COMMITTEE OF THE

PRIVY COUNCIL FOR MEDICAL RESEARCH

REPORT

OF THE

MEDICAL RESEARCH COUNCIL

FOR THE YEAR 1921–22

LONDON
PUBLISHED BY HIS MAJESTY'S STATIONERY OFFICE
1922

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The Medical Research Council.

The Viscount GOSCHEN, C.B.E. (*Chairman*).
The Lord MILDMAY OF FLETE, P.C. (*Treasurer*).
WILLIAM GRAHAM, LL.B., M.P.
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Sir WALTER M. FLETCHER, K.B.E., M.D., Sc.D., F.R.S. (*Secretary*).

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REPORT

OF THE

COMMITTEE OF THE PRIVY COUNCIL FOR MEDICAL RESEARCH

FOR THE YEAR 1921–1922.

TO THE KING'S MOST EXCELLENT MAJESTY IN COUNCIL.

MAY IT PLEASE YOUR MAJESTY,

We, the Lords of the Committee of Your Majesty's Privy Council for Medical Research, humbly submit to Your Majesty a Report of our proceedings during the year ending on 30th September 1922.

1. A Grant-in-aid of £130,000 was provided by Parliament for the whole expenditure of the Medical Research Council during the present financial year, including the cost of the work of the Industrial Fatigue Research Board, and including the grants formerly made to the Board of Control (England and Wales) for the promotion of researches into mental disorders and to the Board of Control for Scotland for pathological inquiries of a routine kind.

2. It was a gratification to us to learn that the Committee on National Expenditure appointed in the past year by the Government recommended that this grant-in-aid proposed by the Treasury for medical research should not suffer reduction. Sir Eric Geddes and his colleagues reported as follows: 'We are assured that the work of this Council in preventive medical research produces very substantial economies in administrative services falling on other Departments, and at a time when the prevention and combating of disease and the alleviation of physical disability is a matter of such vital concern from an economic as well as from a humanitarian point of view, we do not feel justified in recommending any reduction of a grant-in-aid of medical research conducted by a body of selected specialists.'

3. The estimates of the Council for the present financial year, revised after experience of their actual expenditure during the half-year of work ending on 30th September 1922, are being met by our provisional allocation of funds under the following heads.

For administration, including expenses of the Council, of the administrative offices and staff, and of travelling, we have provided £8,000.

For the expenses of the National Institute for Medical Research at Hampstead, for the salaries of the scientific staff there and the expenses of research work done by them or by other workers attached temporarily to the Institute, we have provided £34,000.

For research grants to scientific men and for the expenses of their researches in specific subjects, including mental disorders, at the Universities and at other centres of work in the United Kingdom, for research work in Clinical Medicine, and for the investigations of the Industrial Fatigue Research Board, we have provided in all £88,000.

4. We have received a Report of the Medical Research Council upon the progress of their work during the year ending 30th September 1922, this being the Eighth Annual Report upon the medical research work falling now to their duty and formerly to that of their predecessor, the Medical Research Committee, appointed under the National Health Insurance Act, and this is submitted herewith.

5. In this Report it will be noticed, as on previous occasions, that in the distribution of moneys in aid of scientific researches at the Universities, Hospitals, and other research institutions in the United Kingdom, the Council have continued to delegate many functions of initiation and supervision to various Boards or Committees appointed for particular directions of scientific work.

We desire here to express again our sense of the important services which have thus been rendered gratuitously by the distinguished members of these advisory bodies who are named in the accompanying Report. The Medical Research Council have made it clear, in their account of their own schemes now here presented, in how many different directions they are indebted to these numerous scientific colleagues for the proper discharge of their own public responsibilities.

6. At the National Institute for Medical Research at Hampstead, the Council have again centralized particular parts of their research schemes under their more immediate direction. Among these they have continued to promote researches aimed at securing improved methods for estimating the quantitative and qualitative values of biological substances used either in medical research work or in the preventive and curative work of the medical profession. As at the National Physical Laboratory in other directions of work, so here at the National Institute in the biological field of medicine, studies of methods of measurement and assay and the determination and preservation of standards are a primary part of its contribution to scientific progress.

During the past year we have approved the action of the Council in purchasing a site for Field Laboratories near Mill Hill,

at which necessary facilities for the work of the National Institute can be provided.

7. The work of the Council, as their Report makes plain, has been brought at many points into effective relation to that of the various Government Departments, wherever this has been appropriate, and in many instances research work has been undertaken by the Council at the direct request of a Department seeking a solution for special problems of its own. With the Ministry of Health especially, and with the equivalent Departments for Scotland and Ireland, the closest relations have been maintained, as in previous years.

8. The Council have referred in their Report to the arrangements which have been made in the past year by direction of the Government for periodic conferences between representatives of the Council and of the Development Commission and the Department for Scientific and Industrial Research, for the discussion and adjustment of work done near the boundaries of their respective spheres of action. One of the two secretaries of the Royal Society is invited to attend and take part in these conferences.

9. It will be apparent from the Report which is now submitted how widely extended are the fields of work in which investigation, properly described under the head of medical research, is now conducted. As knowledge has advanced during the last generation the scope of medical inquiry has greatly widened, and there is now hardly any branch of physical science of which the methods and results are not brought in some measure to contribute to the advance of medicine. In the account here given by the Council of work actually in progress during the past year, it will be seen that researches bearing directly upon the advancement of medicine have included many within the domains of pure physics and chemistry, they have strayed into special fields like those of geology and meteorology, and they have ranged through all the parts of modern study in physiology, biochemistry, pathology, and parasitology, using every variety of technical method.

This widening of the scope of inquiry would have been witnessed no doubt even under a narrow and discarded interpretation of ' medicine ' as a study only of disease and abnormality. The conception of medicine itself has at the same time widened in the modern view. It is now concerned not only with the palliation and removal of disorder and pain, but with the prevention of disease, with the maintenance of health no less than with its restoration, and with the choice of conditions in which the bodily machinery of mankind can develop most harmoniously its fullest powers. The results, near and remote, of the industrial revolution have inevitably brought innumerable problems for solution in the light of increased medical knowledge of this wider kind. To this social and industrial ' medicine ' again, in its extended scope, there are few indeed among all the natural sciences which have not their contribution to make.

10. Within this widened field of work we are satisfied that the Council have been able only by the exercise of rigorous choice and elimination to bring their schemes of research within the financial limits imposed upon them. Many suggestions of a valuable kind for new research work, whether from scientific men or expert committees, or whether arising from the needs of Government Departments, have been necessarily deferred or adopted only in part. It is true that the Council have represented to us on former occasions that in some directions of work the limits are set rather by the supply of available and fully competent men than by want of money, but this is by no means always so. We are confident that the Council have exercised to the best of their powers the most effective economy of their resources, and we are satisfied, too, that until these resources can be increased from public funds or by private benefactions, the Council must continue to omit the promotion of much research work of undoubted value.

It is useful in a general survey of this work to consider it in its place as a part only of the general body of researches prosecuted throughout the country. We have been glad to know that the Council have endeavoured so to adjust their schemes as to secure the best co-operation with other directions of effort in the research field, which depend either upon ancient endowments in the Universities or upon more modern benefactions. At very many points in the accompanying Report evidence will be found of this co-operation and interlocking of researches promoted by the Council with other research work supported in other ways, and at the same time with the University systems of higher teaching. From the purely financial standpoint, the grant-in-aid at the disposal of the Council is only a small contribution from the State which meets and augments the provision not only of men but also of money, of buildings and of equipment, derived from private sources, old and new, within the country. The effective value of this public contribution gains from two circumstances. It gains from its mobility, from opportunity to opportunity as any arises at any point within the existing national installation. It is greatly enlarged, too, by this partnership with private effort ; without this it could only have supported effectively a far narrower range of research work than that which this Report displays.

It is considerations of this kind that give us special cause to welcome the references made by the Medical Research Council, in the concluding pages of their Report, to the important benefactions which have recently come from both American and British sources of private origin to promote the advancement of medical sciences in this country.

SALISBURY,
Lord President.

WALTER M. FLETCHER,
Secretary.

19th December 1922.

REPORT

OF THE

MEDICAL RESEARCH COUNCIL

FOR THE YEAR 1921–1922

To the Lords of the Committee of the Privy Council for Medical Research.

May it please Your Lordships,

The Medical Research Council beg leave to submit the following Report upon the work done during the year from 1st October, 1921, to 30th September, 1922.

I. INTRODUCTION.

The grant-in-aid put at the disposal of the Council for the purposes of medical research during the current financial year was £130,000, or the same as the grant-in-aid made for the preceding year ending 31st March, 1922. This grant was again inclusive of provision for the work of the Industrial Fatigue Research Board. It included provision also for the research work into mental disorders done on behalf of the Board of Control for England and Wales and for certain pathological inquiries conducted in Scotland for the equivalent authority there. The work done under these additional heads will be mentioned in its place in the present Report.

In their last Annual Report the Council gave an account of the difficulties which have confronted them in bringing the cost of the work which they support within the limits of their grant-in-aid. This need not, perhaps, be repeated here, though again the Council, while exercising every practicable economy, have found it necessary to restrict their work very closely at many points where increased development would have been highly desirable.

Arrangements have been made in the past year, by direction of the Government, for periodic conferences between representatives of the three departments chiefly concerned in the allocation of moneys voted by Parliament to particular directions of scientific inquiry, namely, the Development Commission, the Medical Research Council and the Department of Scientific and Industrial Research. At these conferences, of which it is proposed to hold

at least one in each quarter of the year, a Secretary of the Royal Society is invited to attend and to represent the Society, in so far as its interests, whether those in relation to the Government grant which it receives for research purposes or those of other kinds, may be affected by or have a bearing upon the policies or programmes of the three research departments. Two of these conferences have already been held. They have proved to be valuable in the interest and the stimulation that they bring; they will no doubt always tend to suggest useful adjustments of methods and of schemes of work. They will maintain the collaboration of the four bodies taking part in them, hitherto secured by the practice of informal and frequent consultations which had long preceded—as it will still accompany—this more regular and formal procedure.

The Council were glad to give, at the request of the Health Section of the League of Nations, all possible assistance to the International Conference summoned on behalf of the League to meet in London in December, 1921, to consider the means to be taken towards the establishment of an international system of common standards for estimating therapeutic sera and other substances used in medical practice or medical research which are susceptible of measurement only by indirect biological methods. At this Conference plans were laid for the conduct of further researches needed in many directions before standards can be securely based, and reports upon work already done have been made to a second Conference in Paris held in November of this year. Further reference to work in this direction under different heads will be made in the present Report. It is interesting to notice that representatives of Germany, of the United States, and of Russia have attended these Conferences inaugurated by the League of Nations. Great Britain unfortunately is alone among the great nations in having no system of standards of her own and no machinery for selecting or adopting any standard of value for a given substance. We are still dependent on the United States or Germany for such standards of reference as are already in use in this field of work, and on several occasions the Council have drawn attention to this situation as being discreditable to our national position in the world of science and a source of grave danger to the community. It may be mentioned that as a result of the last Conference an agreement has been reached by which the standards formerly laid down for diphtheria and tetanus toxins (and antitoxins) by France, the United States and Germany have been recommended for adjustment and general international adoption.

As to the scientific work of which the Council have now to give a summary account, they have little to say by way of preliminary comment. As in previous years there is the same tale to tell, of a large body of work done by devoted workers at many places. The efforts of these investigators have been assisted in a great

variety of ways, and in many instances their work has only been made possible by grants made from the funds at the disposal of the Council. In all this work there have been, as there must be in all honest investigation, many failures, abundant disappointment, and occasional success. Even when success has been reached, it is often only demonstrable to those equipped for understanding it. Success as shown in practical fruit immediately obvious to the layman must always be relatively rare, though success of this kind when it comes has a value in permanence for the community incalculably disproportionate to the small financial cost which the community as such may have contributed. It is only by steady growth of the whole body of sound knowledge, through labours of which the methods and results are not easily understood and appreciated by the people, that practical fruit can be gathered from time to time in the better attainment of health under modern conditions of life and in the better control of disease. In maintaining and more effectively directing the support which they have been enabled to supply in aid of this scientific work the Council have again been under very heavy obligation for the abundant and ungrudging help they have received from the numerous scientific men who assist them in Committees. Of this they would again pay here the fullest recognition.

It will be noticed that no large place in the various schemes of research to be summarized below is given to the investigation of cancer in its many forms. Private endowment and subscription have done more perhaps to support investigation in this subject than in other directions in which better knowledge is also an urgent need. The Council in framing their own schemes of work have not encroached upon the directions of research already being conducted to valuable effect on behalf of the Imperial Cancer Research Fund. This, with cognate work under special endowment at the Middlesex Hospital or elsewhere, they have only endeavoured to supplement when individual workers have sought help to follow particular clues. It will be observed at the same time that the Council have also organized work, to be described in more detail below, at a number of selected hospital centres where radium held by the Council for the Government is being used upon loan for the study of its influence upon cancer and other morbid growths.

During the past year the Council have given close attention to the possibilities of organizing more thorough inquiry into the group of diseases, including many of the common fevers, of which the causative agent appears to be not a microbe of the more familiar kind whose conditions of growth are known at least in part and whose structure is visible under the ordinary microscope, but instead a 'virus' capable of passing through a fine filter, of which the conditions of growth are hardly known at all and whose structure is not visible by the ordinary microscopic methods. The infective agents of diseases like measles, chicken-pox, infan-

tile paralysis, and many others, are probably filterable viruses of this kind, and many believe that to these must be added influenza, scarlet fever, and at least some forms of the common 'cold'. The Council recognize that for new progress in this field every effort must be made to enlist new weapons in the shape of new technical methods of investigation. They hope that some of these may result from co-operation in their National Institute and outside it between biochemists, physicists and pathologists who have been selected for the work, and that these studies may be brought into increasingly effective union with work which has been arranged at fever hospitals under the Metropolitan Asylums Board and elsewhere.

Some inquiries already in progress as part of this scheme will be mentioned further below. Among these will be noticed work by Dr. Gordon at St. Bartholomew's Hospital which has given evidence confirmatory of results obtained in the Army Medical Service during the war, and more recently at the Rockefeller Institute, to show that a 'filterable virus' is the causative agent of influenza, considered in its primary or simplest form and apart from the numerous secondary infections which contribute so commonly to its gravity and mortality. If this be true for the infection of influenza, it is very probably true also for that of common colds. There could hardly be a set of problems whose solution has more potential importance for the community than this. Influenza kills regularly, though its slaughter is chiefly effected during epidemics. In a few months in 1918–1919 it killed more persons in India than had died from plague there during the previous twenty years. Common 'colds', while regularly inflicting widespread suffering and great economic loss, have undoubtedly a very high mortality though it be in large part concealed or indirect. The chief difficulty which the investigator of these problems meets is the difficulty of proceeding by sound experimental methods. It is uncertain whether influenza is transmissible to other animals than man, and in man it is not practicable to make experiments devised so as to give decisive results. Volunteers have on occasion offered themselves for experiment, but volunteers in sufficient number are not likely to be available for submission to rigid conditions of quarantine, experimental infection and isolation, and progress without these is only possible by indirect and imperfect methods of observation and induction.

For reasons of this kind the Council have made arrangements within this part of their programme for an experimental study of distemper in dogs. There is good reason to think that this offers a close parallel to human influenza. It seems probable that the infective agent is a filterable virus, and that here also the severity of the resulting disease depends largely upon secondary infections, facilitated by the primary infection. There is ground for hope that the study of dog's distemper under strict experi-

mental conditions may throw important light upon analogous problems of human disease, and at least suggest new clues for investigation or new technical methods for the investigator. It is with the primary object of gaining knowledge of human disease that the Council decided to support further study of distemper in dogs. On that ground alone they find complete justification of the expenditure of part of their funds in this direction. It need not be said, however, that they also look forward to what from their own point of view must necessarily be a secondary object, namely, the possibilities of relieving or preventing this malady in dogs, and of reducing the great economic loss which it brings to the country. The Council have already received assurances that independent financial support will be forthcoming to meet the special cost of this investigation.

The illustration just given of the close relations between animal and human disease is only one taken from innumerable other instances of the same kind in almost every part of the field of medical work. The science of human pathology has indeed only reached its present imperfect state by experimental studies of animal pathology in the laboratory, combined with observation of the parallel phenomena in man. These studies, however, have had chiefly for their inspiration some direct attack upon particular problems of human disease. Such studies of naturally occurring animal diseases as have been made have often assisted human medicine in the past, and there can be no doubt that a more regular and systematized investigation of animal diseases by well-trained and adequately paid research workers would produce results of value which at present can only be guessed. These results would be shown in diminution of a preventable economic loss from animal disease which is well known to be enormous. Quite apart from that, however, the Council believe, and have long believed, that earlier progress made in animal pathology could not have failed to bring great benefits to human medicine, and they are constantly aware in their own work of the handicap under which they suffer from having no parallel organization for the investigation of animal disease with which they could work in co-operation. On this account they have welcomed the Report of the Advisory Committee on Research into Diseases in Animals appointed by the Development Commission, published in February last, in which the Committee strongly recommend a new organization and a more active policy for the better promotion of research into animal diseases in this country.

It will be seen, however, in the following account of work during the past year that even under present conditions the investigations supported by the Council touch intimately at many points the problems of animal disease. This is notable of course in schemes of work upon tuberculosis, where human pathologists have traced the variety and degree in which tuberculous infections of the cow bring, by way of milk, so much disease of

the bones, joints, and other organs in children. A Committee of the Council have been working throughout the year at improved methods for making the tuberculin tests more effective for cattle, and the same studies by the same men are aimed also at improvements in the use of tuberculin for diagnosis or treatment in human beings. Another worker for the Council in the course of other studies has discovered during the past year the exact mode of transmission of a particular trypanosome infecting the blood of sheep. The Council again have assisted during the year in the elucidation of the first recorded instance of botulism in this country, in the food poisoning tragedy at Loch Maree last August. Work previously done in 1918 for the Armies in France gave important guidance towards the provision of an antitoxin from horses for curative use in the recent outbreak of grass-sickness among horses in Scotland and elsewhere. The success of this antitoxin against grass sickness, and the fact that it is produced in the horse by use of the very toxin which causes botulism in man, illustrates again the vital need for close co-operation between the veterinary and medical sciences and between the pathologists in either field. Indeed, the fields are not merely contiguous ; they cover one and the same territory. The biologist can hardly conceive of true progress in pathology which is not progress in comparative pathology.

The Council have followed with the closest interest, of course, the interesting work upon the treatment of diabetes by extracts of pancreas, which has been done during recent months in the University of Toronto by Dr. F. G. Banting and his fellow workers, with the advice and co-operation of Professor J. J. R. MacLeod in the University Department of Physiology. By the courtesy of the University and at the cordial invitation of these scientific men, representatives of the Council visited Toronto last autumn, and other centres of work to which the Toronto investigations have extended. In this treatment, extracts made from the pancreas of the ox, sheep, or pig have been successfully applied to the relief of diabetic patients whose sufferings come from deficiency in their own pancreatic activity. Relief from semi-starvation, with the prospect of a useful and longer life, has been given already to many sufferers and there is every ground to hope for such improvements, through further research work, of the methods employed as will bring this remedy, known as insulin, to wider use and increasing effectiveness. To meet the difficulties of an exceptional situation and to safeguard the public interest, the University of Toronto have applied for patent rights in the product insulin and the processes of its preparation both on the American continent and in Great Britain. The University have been good enough to invite the Medical Research Council to undertake in this country the responsibilities for the control and development of this product which the University is exercising elsewhere, and they have offered to convey as a gift to the Council

their patent rights in this country. The Council have accepted this generous offer and would here express their gratitude to the University for this gift and for all the other courtesies they and their representatives have received at the hands of the University.

The Council have taken immediate measures for the encouragement and support of research work within the National Institute and at several hospitals in London and elsewhere, with a view to making a supply of insulin available for use in this country as rapidly as possible and promoting further improvements in its production and medical use. They must report on the next occasion upon these and upon other steps they may be able to take. Here they can only briefly point to the great scientific and practical interest of this new work. Admirable and ingenious as this Canadian work has been, the production of insulin and its successful use for the removal of suffering is essentially a technical achievement by which at last a large body of existing knowledge has yielded practical results in a given direction, long foretold and expected. The body of knowledge which has led at last to this practical achievement has been slowly built up during the past generation by patient experiment and observation in the laboratories of many countries, by no means least in those of this country. This work has gone on unseen by the public, and has often perhaps been decried as academic and fruitless. No better illustration of what has been said in an earlier paragraph can be found indeed than this. Physiological science has for many years had this boon in potential readiness for diabetic patients, and indeed the very word 'insulin' now used was given long ago by Sir Edward Schafer in this country to the active principle known to exist. It needed, however, a further technical development before insulin could be prepared for practical use, and this has now come from the devoted labours of Dr. Banting and his colleagues. It must be gratifying to many that this success has come within one of the Canadian medical schools, of which the development and growth in recent years has been so notable, and that so conspicuous an achievement should have come from a group of young men whose eager military service during the War must at many points have brought handicap to their scientific work.

II. THE NATIONAL INSTITUTE FOR MEDICAL RESEARCH (HAMPSTEAD).

An account of the principal work done during the year in the various departments of the Institute is given below under separate heads. Some of the departments have also shared in the investigations which are now being developed with a view to the determination of biological standards and to the devising of methods of biological measurement and assay: this work is discussed separately in Section IV of the Report. Many members of the Institute staff have also taken part in the work of the various special Committees, and this is mentioned in Section V under the various Research Schemes of which an account is given.

The arrangement with the Air Ministry by which the Royal Air Force have occupation of buildings in the Institute grounds for the work of testing and selecting candidates for commissions has been continued for a further period, and laboratory accommodation has again been provided for the Research Pathologist to the Metropolitan Asylums Board, Dr. W. Mair.

It may also be mentioned here that the Council have recently been able to provide improved facilities for the work of the Institute by purchasing a small site for field laboratories outside the metropolitan area but within easy reach of Hampstead. This step has long been contemplated by the Council, and the lack of this kind of accommodation has been greatly needed. In its absence it has hitherto been necessary upon occasion to make more expensive special arrangements elsewhere for particular pieces of work. The need for field laboratories in close effective touch with the Institute has recently become more urgent, especially for the success of the scheme of investigation of infectious diseases believed to be caused by ultra-microscopic organisms or 'filterable viruses' already mentioned on an earlier page. The work in this subject will certainly require facilities for isolation and study which are impossible within the limits of the Institute itself.

The position of the Publications Department within the Institute has served more than administrative convenience. It is linked closely with the Library here and the Department gives invaluable assistance to scientific workers, both within the Institute and outside it, by the supply of references to published papers and of other information, and by the preparation of diagrams and figures for press reproduction. This work effects great economy of time and of money. It happens by a fortunate coincidence that Dr. Edgar Schuster, in charge of the Department, is highly skilled in the arts of mechanical design and construction. He has devised and executed in his spare time many pieces of scientific apparatus for use in the research work of his colleagues, and to some of these reference will be made below. The Council

are greatly indebted to him for regular service, beyond his normal duties, in advising upon the design of all mechanical apparatus constructed in the Institute for work within it or outside.

Biochemistry and Pharmacology.

Staff—
H. H. Dale, C.B.E., M.D., F.R.S. (*Director*).
H. W. Dudley, O.B.E., M.Sc., Ph.D.
Harold King, D.Sc.
J. H. Burn, M.A., M.B.
Miss F. M. Durham.
Miss J. E. Marchal.

Dr. Lovatt Evans has left the department upon his appointment in March to the Chair of Physiology at St. Bartholomew's Hospital. During the period of his work at the Institute, he has been doing work of fundamental importance on the acid-alkali balance of the blood and the factors influencing it. He has also acted as Secretary to the Haemoglobin Committee, whose report on the problems of blood-reaction is nearing completion (p. 93). Dr. Dale and Dr. Evans have completed and published the results of their joint work on the influence of carbon dioxide upon the maintenance of normal blood circulation. The effect on the tone of the vasomotor centres has been shown to be a specific action of carbonic acid, as distinguished from the chemical reaction (hydrogen-ion concentration) of the blood.

Dr. Dale and Dr. C. H. Kellaway (Foulerton Student of the Royal Society) have completed and published an investigation of Anaphylaxis and the relation to it of the so-called 'Anaphylatoxins'.

Dr. Burn has published the results of his work on the relation of the sweating produced by the drug pilocarpine to the integrity of the nerve-supply of the sweat-glands. There has for many years been a puzzling discrepancy between the experimental evidence, according to which the response of the sweat-glands to pilocarpine is independent of their nerve-supply, and the clinical observation that the extent of a nerve injury can be detected by the failure of pilocarpine to produce sweating in the corresponding area of skin. Dr. Burn's experiments show that the sweat-glands give an undiminished or even increased response to pilocarpine after the degeneration of their intrinsic 'sympathetic' nerve-supply, but that the concomitant degeneration of the sensory nerve-fibres to the skin area in question is usually attended by great diminution or suppression of the sweating response. He brings forward evidence strongly supporting the conclusion that this impairment of the glandular response is the result of defective blood circulation caused by the loss of the sensory fibres, and his results raise issues of great importance concerning the so-called 'trophic' or nutritive influence of sensory nerves. It is to be

hoped that further developments of the suggestions so given will be found possible.

Dr. Dudley has devoted a large part of the year to the refinement of products obtained from the large supply from America of dried material of the posterior lobe of the pituitary gland which has been mentioned in previous reports. The results, although highly instructive, discourage any hope of the early isolation and identification of the active principle of the pituitary gland in pure form. They strengthen the earlier evidence of the extraordinary intensity of the action of the substance concerned. A crystalline picrate was isolated which, after several recrystallizations, showed an action upon uterine muscle of about the same order as that of so intensely active a substance as histamine. But this proved, on ultimate purification, to be an inert substance—the double picrate of potassium and creatinine—to which a mere trace of the true active principle had been adherent. It seems quite clear that principles having an activity of this order—such that the whole activity of a kilogram of the costly gland substance might be represented by a few milligrammes of the pure active principle—will not be directly isolated and identified by methods at present available. The problem of obtaining these, and probably the hormones of several other glands in a pure form, with a view to their identification and artificial production, needs the development of a completely new biochemical technique. Meanwhile this attempt to isolate the pituitary principles, a full account of which is in course of publication, has furnished valuable experience towards dealing with substances of this type, and this may soon find application in studies of the new treatment of diabetes by a pancreatic hormone, introduced by Banting and Best, working in Professor MacLeod's department at the University of Toronto (p. 14). It may be added here that Dr. Dale and Dr. Dudley visited Toronto this autumn, on behalf of the Council, to study this new development in the laboratory and hospitals where it originated.

Dr. King, whose work with Major Acton on quinine was mentioned in the last Annual Report, has just completed a study of stereoisomerism in the cinchona alkaloids. He has also carried out an investigation of muscarine, the active alkaloid of the poisonous toadstool, *Amanita Muscaria*, which has long been a subject of controversy. The material available was sufficient only to prove that all previous conceptions of the nature of muscarine, and of its relation to choline, have been erroneous, and have sprung from the fact that the materials subjected to analysis have consisted chiefly of choline, merely contaminated with varying proportions of the really active muscarine. The problem is now within sight of solution, only an adequate supply of the *Amanita* being required. Dr. King's papers on the cinchona alkaloids and on muscarine are in course of publication.

The other work of the department falls chiefly within the scheme of research in Biological Standardization, of which some

account is given in Part IV of this report (p. 41). Further references will be found under the headings of the several special Committees on the Properties of Haemoglobin (p. 93), Malaria and Cinchona Derivatives (p. 94), and the Biological Actions of Light (p. 89).

Publications :—

J. H. Burn.
' The relation of the nerve supply and blood flow to sweating produced by pilocarpine.' *J. Physiol.*, 1922, **56**, 232.

H. H. Dale—
' Specific Sensitiveness and Anaphylaxis.' *Brit. M. J.*, 14th January, 1922.
' The Reversal of Vagus Action by Quinidine.' *Heart*, 1921, **9**, 87.

H. H. Dale and C. H. Kellaway.
' Anaphylaxis and Anaphylatoxins.' *Phil. Tr. Roy. Soc.*, 1922, B., **211**, 273–315.

H. H. Dale and C. Lovatt Evans
' Effects on the Circulation of Changes in the Carbon-dioxide Content of the Blood.' *J. Physiol.*, 1922, **56**, 125.

H. H. Dale and C. F. White, in conjunction with J. H. Burn, F. Durham, J. Marchal, and C. H. Mills—
' Report on an experimental and clinical comparison of the therapeutic properties of different preparations of '914' (Neosalvarsan).' *Lancet*, 22nd April, 1922.

J. H. Burn and H. H. Dale—
' On the Physiological Standardization of the Posterior Lobe of the Pituitary Body.' *M.R.C., Special Report Series*, No. 69, 1922.

H. H. Dale and K. Spiro—
' The Active Alkaloids of Ergot.' (In course of publication.)

H. W. Dudley—
' On the Active Principles of the Pituitary Gland.' (In the press.)

H. King—
' Fine Chemicals, Medicinal Substances and Essential Oils.' *Annual Report of the Society of Chemical Industry.* Vol. VI, 1921.
' The Isolation of Muscarine, the Potent Principle of *Amanita Muscaria*.' *Trs. Chem. Soc.*, 1922, **121**, 1743.

H. King and A. D. Palmer—
' The Resolution of Tropic Acid and the Stereochemical Configuration of the Cinchona Alkaloids.' *Trs. Chem. Soc.*, 1922, **121**, 2577.

C. Lovatt Evans—
' Acid Production in Shed Blood.' *J. Physiol.*, 1922, **56**, 146.

E. H. J. Schuster—
' A Simple and Double Action Respiration Pump.' *Proc. Physiol. Soc. J. Physiol.*, 1922, **56**, x.
' An Automatic Recorder of Oxygen Consumption.' *Ibid*, 1922, **56**, xxv.

Experimental Pathology, Bacteriology, and Protistology.

Staff

Captain S. R. Douglas, M.R.C.S., F.R.S., late I.M.S. (*Director*).
W. E. Gye, M.D.
Clifford Dobell, M.A., F.R.S.
P. P. Laidlaw, B.Ch.
Leonard Colebrook, M.B., B.S.
Percival Hartley, D.Sc.
W. J. Purdy, M.B.

Attached

W. H. Tytler, M.B.

The staff of the department has recently been increased by the appointment of two new workers, Dr. P. P. Laidlaw, formerly Dunn Professor of Pathology at Guy's Hospital, and Dr. Percival Hartley. Dr. W. J. Purdy, previously an attached worker at the Institute, has also joined the staff. On the other hand, the department has temporarily lost the services of Dr. Colebrook, who is now assisting in Sir Almroth Wright's work (p. 96) in the Inoculation Department of St. Mary's Hospital, while Dr. Gye's work has unfortunately been much interrupted by ill health during the year. Dr. Tytler has now left to take up an appointment in the Welsh National Medical School.

Captain Douglas's own time has been much taken up by his special duties as Director of the department, as Secretary of the Bacteriology Committee (p. 83), and as Chairman of the Sub-Committee on Tuberculin (p. 77), and most of his research during the past year has been upon problems arising from the work of these committees. For the Bacteriology Committee he has been engaged in special studies of the cultivation and isolation of the diphtheria bacillus. This work has resulted in the production of a new medium giving certain advantages over Loeffler's medium at present almost universally employed. The new medium is transparent instead of opaque ; the colonies of *B. diphtheriae* and some allied organisms present a distinctive appearance to the naked eye and the growth of the commonly associated organisms is inhibited, and it has further useful qualities as other workers have already found. A full account of the medium, and of the results obtained by its aid, will shortly appear in the *British Journal of Experimental Pathology*.

In conjunction with Mr. Barnard (p. 27) a number of observations have been made by Captain Douglas on the structure and measurements of bacteria both living and dead, stained and unstained. These are only preliminary, but the results obtained indicate that this line of research will be a fruitful one.

For the Committee on the Biological Actions of Light (p. 89) some preliminary experiments were also made to ascertain if overdoses of light rays tend to allow the tissue of resistant animals to be invaded by bacteria. These experiments were made on rats, and it was found that when tubercle bacilli present in the skin received the application of light on a shaved area a progressive lesion was produced in a considerable percentage of the animals, while, in the case of animals not exposed to the action of the rays, the ordinary regressive lesions commonly seen in the rat were present. The source of light employed was the mercury vapour lamp. The strain of tubercle bacillus was one of the human type, and the presence of a small quantity of haematoporphyrin solution in the area infected with the tubercle bacillus was found to have an intensifying action upon the light effects, which received special study.

Attempts have also been made by Captain Douglas to ascertain

the thermal death-point of tubercle bacilli occurring in naturally infected milk. Previous observations on this point have been contradictory; many have been made with artificially infected milk, and the results are not fully applicable to naturally infected milk. These experiments are not yet complete, but it appears to be certain that a temperature of 65° C. for thirty minutes will kill the tubercle bacilli in naturally infected cow's milk.

Captain Douglas has undertaken, further, a number of experiments to attempt to find out whether and how closely human and rat leprosy are related. A naturally infected leprous rat was obtained through the kindness of Mr. J. B. Tutt, F.R.C.V.S., of Winchester, and material from a human leper through Dr. Colebrook. Taking advantage of Dr. Laidlaw's work on the stimulating effect of various extracts and ferments on bacterial growth, attempts are being made to cultivate artificially for the first time both human and rat types of the leprosy bacillus for better study. The results of these attempts are also at present undecided.

The work in which Dr. Gye has been chiefly engaged has been the continuation, with Dr. Purdy, of the study of the poisonous properties of colloidal silica, hitherto believed to be harmless, and during the past year much new information has been gained. This careful investigation of the pharmacology of colloidal silica was thought desirable, not only for its great theoretical interest, but also because the substance has been, and is still being, used as a drug in Germany in the treatment of tuberculosis and arteriosclerosis. Other work by Dr. Gye and Dr. Purdy has been a study of the physiological properties of certain other simple organic salts.

With Dr. E. H. Kettle of St. Mary's Hospital, Dr. Gye has completed and published studies of the effects of silica dust upon the tissues, with special regard to the problems of industrial tuberculosis. They have thoroughly investigated also the experimental basis of the treatment of tuberculosis with soluble silica which some have recommended. They have found that colloidal silica fed to or injected intravenously into susceptible animals has no influence on the progress of tuberculosis: the only influence it has is upon the establishment of a localized infection where the lesion caused by silica—soluble or insoluble—is such as to provide a *nidus* in which the tubercle bacilli, protected from the bactericidal defences possessed by the normal tissues, can multiply and so initiate progressive damage. Thus a very small dose of bacilli given with silica becomes in effect a large one, and the infection becomes firmly established. Dr. Gye and Dr. Kettle have also begun some special studies of the pathology of general tuberculosis in young people.

Dr. Gye's work on disseminated sclerosis, which was temporarily abandoned on account of ill health, has been taken up again with Mr. Dobell.

Dr. Laidlaw began work at the Institute in last May, and was

at first occupied in completing a method for estimating very minute quantities of carbon dioxide in the air. His preliminary experiments at Guy's Hospital had shown that amounts of the order of one-millionth of a gramme could be estimated. The limitations of the method were defined, and it was found that accuracy of that order could not be acquired owing to the impossibility of cleaning glass surfaces. The method can be used to determine readily and accurately the changing carbon dioxide content of atmospheric air, and, for instance, the increase that occurs in fogs. It is also proposed to apply the method, which may have many other uses, to a comparison between the amounts of carbon dioxide given off by nerves at rest and during activity respectively.

Many experiments have also been made by Dr. Laidlaw in attempts to define more closely the factors which favour the growth of pathogenic bacteria. It has been found that some constituent is present in meat extract which is strongly stimulating. Its nature is quite uncertain, and is by some believed to be allied to the vitamins. Experiments are in progress with the object of isolating this constituent. Certain ferments have been found to have a beneficial effect on the growth of organisms, and the preliminary results are being confirmed in a wider and more representative series of bacteria. Work has also been begun to determine the conditions necessary for the cultivation of spirochaetes.

Dr. Hartley, who also began work at the Institute in May, has continued Dr. Colebrook's studies for the preparation of an antitoxic diphtheria standard for use in this country, a subject which is discussed more fully in the section dealing with Biological Standardization (p. 42).

Dr. Colebrook, while still at the Institute, was engaged on the work which he has now handed over to Dr. Hartley, and in some experimental work for the Committee on the Causes of Dental Disease (p. 66). He has studied the artificial erosion of teeth by various methods arranged to simulate natural or common conditions in the mouth, and has investigated the types of acid-loving bacilli occurring in the mouth, and the micro-organisms actually found in carious teeth. A report upon these experiments is in preparation.

Dr. Purdy has continued to act as pathologist to the neighbouring New End Hospital. On the experimental side he has been occupied chiefly in the work in collaboration with Dr. Gye mentioned already : the beautiful illustrations published in their joint papers are from his drawings. He has also supervised or undertaken the histological work of the Institute, of which the amount has been very great.

Dr. Tytler, as already stated, has now brought his work at the Institute to a conclusion. During the year he continued his investigation of the conditions favourable to bacterial growth, using in particular some haemolytic strains of streptococcus

obtained from scarlet-fever cases by Dr. Mair (p. 16). He has studied the stimulating effect of blood-serum in increasing both the rate of growth of these organisms and the final bacterial concentration, and he has examined the conditions in which it may lose its power of increasing growth-rate, but still allow an undiminished final bacterial concentration. The latter, according to previous work with *B. coli*, seems to depend on the concentration of the foodstuff present. An accelerating factor in the serum seems to be independent of the qualities of serum if considered only as foodstuff. Pursuing these studies, he found that solutions of either fresh or crystallized haemoglobin had an effect upon growth more powerful than that of serum: these have been further investigated, with many other substances and tissue extracts, and their modes of action analysed. A main object has been to determine how far these substances yield a necessary type of foodstuff, or whether some or all of them act only as 'catalysts' aiding the utilization by the organisms of other foodstuffs present. Much of this work was done with Dr. Laidlaw, who supplied many of the preparations used.

Protistology.

Mr. Dobell has been preparing for publication an extensive study of the Coccidia, with which he has been occupied since 1908. Another investigation in which progress has been made is that dealing with the theory and practice of staining spirochaetes and other micro-organisms with silver salts. This is a subject of great complexity, but one which, when fully elucidated, promises to lead to results of great practical importance, for this method is valuable for the detection of some of the most minute and elusive micro-organisms. In this work much assistance has been given by Dr. Laidlaw.

The work which Mr. Dobell has undertaken with Dr. Gye on disseminated sclerosis has been continued. This has shown the imperfection of some of the microscopic and cytological methods employed, and much effort has been given to gaining technical improvements without which further progress appears to be impossible. The results so far obtained are promising, and further work on this subject is in progress.

Mr. Dobell was engaged during the earlier part of the year in writing, in collaboration with Colonel D. Harvey, A.M.S., a section upon 'Amoebic Dysentery' for the official *Medical History of the War*. This is now in the press. A series of articles which he wrote, partly in collaboration with Dr. G. C. Low, for *The Practice of Medicine in the Tropics* (edited by Byam and Archibald), has appeared in the course of the year. Other publications from his department include two papers of historic interest—a short biographical note on the life and works of Timothy Lewis and a memoir on the earliest known observations on the Coccidia. This last paper is based upon a study of the

early—and in part still unpublished—Dutch manuscripts of Leeuwenhoek, which have great importance in the history of Protistology.

Throughout the year Mr. Dobell has given assistance to various hospitals and medical practitioners by examining pathological material for special purposes of diagnosis. He has also given special help to various workers, at home and abroad, in the identification of specimens, in the preparation of their scientific results for publication, and in other ways. Among those who have received such assistance may be mentioned Dr. C. Franca (Collares, Portugal), Professor B. L. Bhatia (Lahore), Mr. H. M. Fox (Cairo), Dr. A. Connal (Nigeria), Dr. B. Sokoloff (Brussels), and Dr. Toynbee Wight (Palo Alto, California). Mr. Dobell has also continued to assist the Tropical Diseases Bureau by contributing critical reviews of works of medico-protozoological interest (chiefly Dutch) to their *Bulletin*.

Publications :—

S. R. Douglas—
' A new medium for the growth and isolation of *B. diphtheriae*.' *Brit. J. Exper. Pathol.*, 1922, **3**, 263.
W. Cramer and W. E. Gye—
' Anaerobic Infections.' *J. State Med.*, 1922, **30**, 254.
W. E. Gye and E. H. Kettle—
' Silicosis and Miners' Phthisis.' *Brit. J. Exper. Pathol.*, 1922, **3**, 241.
' The Pathology of Miners' Phthisis.' *Lancet*, 21st October, 1922.
W. E. Gye and W. J. Purdy—
' The Poisonous Properties of Colloidal Silica. I. The Effects of the Parenteral Administration of Large Doses.' *Brit. J. Exper. Pathol.*, 1922, **3**, 75.
II. ' The Effects of Repeated Intravenous Injections ; Fibrosis of the Liver.' *Ibid.*, 1922, **3**, 86.
C. Dobell—
Articles on ' Amoebiasis ', ' Coccidiosis ', ' Balantidiosis ', ' Intestinal Flagellates of Man,' and ' Introduction to Protozoal Diseases ' (partly in collaboration with Dr. G. C. Low) in Byam and Archibald's *Practice of Medicine in the Tropics*. Vol. II, 1922.
' T. R. Lewis (1841–1886).' Biographical Note. *Parasitology*, 1922, **14**, 413.
' The Discovery of the Coccidia.' *Ibid.*, 1922, **14**, 342.
C. Dobell and D. Harvey—
' Amoebic Dysentery.' *Medical History of the War* (Pathology). (In the press.)
C. Dobell and D. Carazzi (Florence)—
' Parole e idee errate in Biologia.' *Rassegna delle Scienze biologiche*, 1922, **4**, 49.

Applied Physiology.

Staff—

Leonard Hill, M.B., F.R.S. (*Director*).
J. Argyll Campbell, M.D., D.Sc.

Attached—

M. Greenwood, M.R.C.S. (*Ministry of Health*).
T. A. Webster.

Dr. Argyll Campbell, formerly attached to the department, has been appointed to the staff. Dr. M. Greenwood, Statistical

Medical Officer in the Ministry of Health, has continued to be accommodated in the Institute and has again co-operated with the Council's staff in many valuable ways, including his chairmanship of the Industrial Health Statistics Committee (p. 105).

Dr. Hill and his colleagues have continued their investigations into various problems of body heat and metabolism, and into the bearing of these upon practical questions of ventilation and upon different forms of open-air treatment for the arrest of tuberculous and other diseases. With Dr. Campbell and Miss Hargood-Ash, Dr. Hill has carried out further studies of the effects of local heating and cooling of the body, especially in relation to the rate of chemical changes within it.

Observations of the rates of internal chemical exchanges in children crippled by surgical tuberculosis and lying fixed in splints in bed at Lord Mayor Treloar Hospital, Alton, were continued by Dr. Hill and Dr. Campbell with the co-operation of Sir Henry Gauvain, to whom, as Superintendent of the Hospital, the Council are greatly indebted for much assistance. The beneficial exposure of the children, more or less nude, to the open air in summer increased these exchanges of metabolism, on an average, to about 40 per cent. above the standard basal figures for closed chambers. Exposure in winter increased the metabolism very much more, of course, than in summer, although in both cases the children were not exposed sufficiently to cause shivering. Evidence was obtained that the rise in metabolism caused by light in heliotherapy *per se* was insignificant compared with that caused by exposure to open air, notwithstanding the value of heliotherapy as a factor in the arrest of surgical tuberculosis. Balneotherapy at the Hayling Island Colony increased by 100 to 200 per cent. the metabolism of the children who were immersed without muscular movement. It was concluded that the treatment used here—open-air, heliotherapy, and balneotherapy—might be applied with advantage to other cases of illness usually involving long confinement in bed.

Observations have also been made by Dr. Hill at the English Sanatorium at Montana, Switzerland, with the co-operation of Dr. Bernard Hudson, at the Belgian clinic under Dr. Chassot, and at the Geneva Sanatorium under Dr. Betchow. The results of exposure to the Alpine open-air under a variety of conditions, as shown in changes in metabolism, were studied. Observations of a similar kind were made at other sanatoria—The Sevenoaks Hip Disease Hospital (Dr. Sichel), the High Carley Sanatorium (Dr. Pask) at Ulverstone, and the Berks and Bucks Sanatorium (Dr. Carling). The Council would thank all these medical officers for their co-operation in these researches and for their hospitality.

A wind tunnel has been constructed at the Institute, by the conversion of an existing long narrow corrugated iron passage to this purpose. It is fitted at one end with a suitable fan so that

a wide variation of cooling powers can be obtained within the tunnel. At the other end a conveyor band or walking platform, electrically revolved, has been inserted in the floor: on this, walking or running at a rate of from 1½ to 8½ miles an hour can be undertaken by the subject, almost stationary in relation to the walls and the observer, and cooling can be effected as desired. Observations by Dr. Hill and Dr. Campbell to determine the amount of cooling necessary for comfort during various degrees of muscular work showed, for instance, that for one hour's work—walking on the moving platform—the cooling power of the atmosphere as measured by the dry kata-thermometer should be twice the heat production of the body expressed in millicalories per square centimetre per second. It was shown that the frequency of the heart-beat was much less when the body was adequately cooled.

With a view to problems of industrial welfare, observations have been made to determine the effects of work during night shift, with sleep during the day. Four consecutive days of this showed that the subjects had not become accustomed to the revised routine. Although they slept well during the day, they felt tired at night and the metabolism sitting at rest was at a low ebb compared with that for similar conditions during the day. Nevertheless, the efficiency with which short spells of muscular work were carried out was not altered. Dr. Campbell and Mr. Webster found that there was an absolute increase in urinary phosphate during the reversed routine; this was considered to be connected in some way with sleep, since under various routines the higher figure for phosphate, whether found by day or by night, always accompanied sleep and could be separated from every other factor but sleep. Dr. Campbell and Mr. Webster also noted that there was a fixed excretory rhythm in which there were tides of water, nitrogen, urea, and chloride during the day and tides of phosphate, ammonia, and titratable acid during the night. This rhythm was not changed by various changes in the routine. In the reversed routine, in which the food and fluid were taken at night, the water excretion and total nitrogen excretion were still higher during the day; in this routine, work was done at night and sleep taken during the day.

Some inquiries have been made by Dr. Hill and Dr. Campbell into the rate at which the composition of air changes when injected into a pleural cavity as in the treatment of consumption by the production of artificial pneumothorax. In these they have had the co-operation of Dr. Clive Riviere. The carbon dioxide is found in the first few minutes to increase quickly, while the oxygen lessens more slowly. The partial pressures of the gases in this air appear to approximate finally to those in the tissues and venous blood and not to those in the alveolar air of the lungs. Studies of the capillary circulation are being continued by Dr. Leonard Hill, with Mr. J. D. Malcolm in order to

determine the sequence of changes in the small vessels which occur during the induction of shock.

A report has been prepared by Dr. Hill upon the kata-thermometer as an instrument of precision, upon its use in factories for the regulation of ventilation and human efficiency, and upon human metabolism in relation to the cooling power of the atmosphere. To this report, Dr. Campbell, Miss D. Hargood-Ash and Dr. H. M. Vernon (p. 108) have contributed. The last has added an analysis of the numerous investigations carried out by workers of the Industrial Fatigue Research Board. This report, it is hoped, should prove of value to all who are using the kata-thermometer for the measurement and control of ventilation and the management of open-air treatment.

In addition to the researches already mentioned the staff of the department have participated in the investigations now being undertaken for the Committee on the Biological Actions of Light (p. 89).

Publications :—

Leonard Hill, D. Hargood-Ash and J. Argyll Campbell—
'On the Heating and Cooling of the Body by Local Application of Heat and Cold.' *Proc. Roy. Soc.*, 1922, B., **93**, 207

Leonard Hill and J. Argyll Campbell—
'Metabolism of Children undergoing Open-air Treatment, Heliotherapy and Balneotherapy.' *Brit. M. J.*, 25th February, 1922.

Leonard Hill and J. Argyll Campbell—
'Observations on the Resting Metabolism of Children and Adults in Switzerland.' *Brit. M. J.*, 11th March, 1922.

J. Argyll Campbell and T. A. Webster—
'Effect of severe Muscular Work on the Composition of the Urine.' *Biochem. J.*, 1922, **16**, 106.

Leonard Hill and J. Argyll Campbell—
'Observations on Metabolism at the Sea-side.' *Lancet*, 8th April, 1922.

Leonard Hill and J. Argyll Campbell—
'The Effect of Atmospheric Cooling Power on the Pulse Rate and on the Efficiency during Muscular Exercise.' *Proc. Physiol. Soc., J. Physiol.*, 1922, **56**, xlix.

J. Argyll Campbell and T. A. Webster—
'Day and Night Urine during complete rest, Laboratory Routine, Light Muscular Work and Oxygen Administration.' *Biochem. J.*, 1921, **15**, 660.

Leonard Hill—
'Ventilation in relation to Cotton Factories' (Chadwick Trust lecture given at Bolton). *Lancet*, 7th January, 1922.
'Clean Air' (Lecture to the Congress of the Royal Sanitary Institute at Bournemouth). *J. Roy. San. Inst.*, 1922, **43**, 67.
'Ventilation and Human Efficiency'. (Lecture to the Institution of Mining and Metallurgy). *Bull Inst Mining and Metallurgy*, 1921-22.
'Science of Open Air Treatment'. *Brit. J. Tuberc.*, 1922, **16**, 72.

Applied Optics.

The Council have again to express their great indebtedness to Mr. J. E. Barnard, late President of the Royal Microscopical Society, for his continued services as honorary director of this

department, which has met many needs of other workers both within the Institute and outside it.

Mr. Barnard's studies for the improvement of microscopical methods has been continued. With a view to reducing the instrumental difficulties met in many kinds of work the whole question of the best microscopical equipment for research work has been considered. The result has been that a new type of illuminant, a new form of microscope, and certain improved optical parts have been evolved : these are now in use and have proved of much service. This apparatus is being further improved in detail and a description of it, with full directions for use, is in preparation and will soon be published.

The methods of dark-ground illumination have also been reconsidered and improved, and a new illuminator used with an improved type of mercury-vapour lamp appears likely to be of special value in the observation of living organisms. A simple method has been devised for the more easy and certain identification of the spirochaete of syphilis by which the number of convolutions in the spirochaete can be quickly determined in reference to the diameter of a red blood cell. The appliance is inexpensive and easy to use, and can be added to any ordinary microscope. A description of it and its method of use will be published in the new edition of the Council's Special Report, No. 19, which is at present in preparation (p. 84). The measurement of microscopical objects has also received attention, in view of the common want of agreement between the micrometric results obtained by different workers describing the same structures. To ensure constancy and accuracy an apparatus has been installed to which any worker in the Institute can refer. So far as possible the usual incidental errors have been provided against, and the results obtained are as accurate as present-day appliances will allow.

In collaboration with Captain Douglas, an investigation of the structure of bacteria has been begun. The structure seen as the result of staining has been carefully compared with photographs taken of living organisms from the same cultures by means of ultra-violet light. The results so far obtained are interesting and suggestive, as showing the changes that are due to the processes incidental to staining.

A simple application of the principle of the ' interferometer ' has been employed to determine quantitatively the strains and stresses in a microscope in the course of use, and to measure the inevitable inaccuracies in fine adjustments. The research microscope already mentioned as at present in use was much improved as the result of the tests applied.

Studies of the use of ultra-violet light in microscopy have been continued with encouraging results. A new and more efficient apparatus is now nearly complete, with which it is expected that results will be obtained with greater certainty and ease than

hitherto. Shorter wave-lengths are now being used, and the results indicate that structures of a smaller order will be resoluble. A number of experiments have also been carried out under the scheme of work formulated by the Committee on the Biological Actions of Light, and these will be reported in due course.

The photographic work of the department has greatly extended during the past year. The processes of development and printing have been systematized to ensure constancy of results and to avoid waste. Photo-micrographs have been produced for approved outside workers as well as for those working in the Institute. Nearly three hundred lantern slides have been made for various lectures and demonstrations. Mr. Barnard has examined and reported upon many microscopes and other optical instruments for general or special purposes.

In view of the growing work of this department the Council have appointed a whole-time assistant, Mr. J. Smiles.

Publications :—

J. E. Barnard—
'The Use of Ultra-Violet Light in Microscopy.' *Dictionary of Applied Physics.* Vol. III. Edited by Sir R. T. Glazebrook, F.R.S., 1922, Macmillan & Co.
'The Future of the Microscope in Medical Research.' *J. Roy. Microsc. Soc.* (In the press.)
W. C. C. Topley, J. E. Barnard, and G. S. Wilson—
'A new Method of obtaining Cultures from single Bacterial Cells.' *J. Hyg.*, 1921, **20**, 221.

Statistics.

Staff—

John Brownlee, M.D., D.Sc. (*Director*).
Matthew Young, M.D.

Attached—

H. L. Trachtenberg, B.A., A.I.A.

During the past year Dr. Brownlee has been engaged in preparing an account of the data necessary for the statistical study of immunity, incorporating the results of work which he has done himself during the last few years. To this account will be prefaced a synopsis of those mathematical methods used in physical chemistry and biology which have a bearing on the subject.

Dr. Brownlee has also been engaged in investigating the relation of scarlet fever to rainfall. The results are being prepared for publication. In addition, the statistics of births and deaths, with special regard to the effects which the falling birth-rate may be expected to produce, have been studied.

Dr. Young has been engaged in various investigations during the past year. He has worked upon the data of the statistics of

epidemic infantile diarrhoea more fully than has hitherto been done and he has extended the investigation to several towns in the provinces and abroad. The results of his work on the distribution of cancer in the Severn Valley, mentioned in previous Reports, have now been published. He has also been occupied in arranging data that have been collected by the Committees for Anthropometric Methods (p. 48) and for Child Life investigations (p. 51), and on these he has written reports.

Dr. Young has also made many experiments on the rates of onset of death and of anaesthesia in some minor crustacea and in tadpoles, with a view to testing the truth or falsity of current interpretations of certain kinds of statistical evidence. It is proposed to carry these investigations farther, because the results so far obtained are of interest and in many respects run contrary to usual opinion.

Mr. Trachtenberg has proceeded with his investigation into the widened scope given to the Gompertz law of mortality, when the change in form consequent on a possible differential application to various types of population is considered. It is hoped that the results may be published during the coming year. He has further considered the method of overcoming difficulties which have presented themselves to statisticians in the fitting of the logarithm, and he has arrived at an effective solution.

Mr. Russell, chief clerk in the department, as a preliminary to further investigations into the relationship between weather and disease, has examined the degree of dependence between two of the weather factors—rainfall and temperature—in successive and alternate months over a series of years for Greenwich, Glasgow, Greenock, and Dundee, by the method of correlation. He has also superintended the calculation of a table of the logarithm of the Gamma function to seven places of decimals for values of the argument from 2 to 40, and he has constructed a table by reference to which, in formulae of the nature of $(x+a)^n$ or $(c-x)^n$, a and c can be readily determined.

By the courtesy of the Registrar-General statistics of the incidence of cancer in different trades have recently been placed at the disposal of the Council and have been extracted by the clerical staff of the Statistical Department. The data refer to 46,235 deaths among males, both occupied and retired, occurring in over 900 trades and professions in England and Wales during the period 1910–12. Particulars have thus been obtained for each trade as to the type of cancer, the site of the growth, and the age distribution among occupied and retired males. This material is to be examined and reported on by Dr. Brownlee in collaboration with Professor E. L. Collis.

Dr. Brownlee and his colleagues have given much time during the year to the critical examination and discussion of statistical work in which their assistance has been sought by research workers in various medical fields.

Publications :—

John Brownlee—

'A Census of Youth.' *Times*, 16th January, 1922.

'Restriction of Birth in Relation to National Weal.' *Lancet*, 29th July, 1922.

'Interpretation of the Death Statistics of Infancy and Childhood in Relation to Development and Environment.' *Brit. M. J.*, 26th August, 1922.

'The Census of 1921 and its Lessons.' *Manchester Guardian Commercial.*, § 6, 1922, p. 345.

'Rainfall and Scarlet Fever.' *British Rainfall.* No. 6138.

'Mortality in Childhood with reference to Hygiene.' *J. Hyg.*, 1922, **21**, 126.

John Brownlee and Matthew Young—

'Epidemiology of Summer Diarrhoea.' *Proc. Roy. Soc. Med.*, 1922, **15** (Sect. Epidemiology), 55.

Matthew Young—

'Some Observations on the Distribution of Cancer in the Severn Valley.' *J. Hyg.*, 1922, **21**, 49.

H. L. Trachtenberg—

'Another Method of Valuing Policies in Groups.' *J. Inst. Actuaries*, 1922, **53**, 61.

W. T. Russell—

'The Relationship between Rainfall and Temperature as shown by the Correlation Coefficient.' *Quart. J. Roy. Meteorol. Soc.*, 1922, **48**, 225.

Library and Publications Department.

The principal additions to the Library during the year have been *Index Medicus*, 1st series : *American Journal of Physiology* from 1910 : *Berichte der deutschen chemischen Gesellschaft* from 1879 : *Journal of Infectious Diseases*, complete : *Journal of the Royal Microscopical Society* complete : certain 'Challenger' Reports : Scientific Memoirs by Medical Officers of the Army in India : Scientific Memoirs by Officers of the Medical and Sanitary Departments of the Government in India, new series : Annual Reports of the Sanitary Commissioners with the Government in India, nearly complete : and Abderhalden *Handbuch der biochemischen Arbeitsmethoden*. About 200 British and foreign periodicals dealing with the medical sciences are being regularly received, and of these 120 are in exchange for *Medical Science*.

The Medical Research Council would here express their gratitude to the following for donations of books, periodicals, and reports :—

Mr. J. E. Barnard, Professor C. H. Browning, Dr. J. Brownlee, Professor W. Bulloch, Bureau of Census, Washington, Carnegie Institution of Washington, Dr. A. K. Chalmers, Dr. H. H. Dale, Mr. Clifford Dobell, Captain S. R. Douglas, Dr. R. Dudfield, Dr. T. Elliott, The Henderson Trust, Dr. Leonard Hill, Dr. E. W. Hope, Dr. R. E. Lauder, Sir George Makins, Dr. J. Wright Mason, Director-General of Public Health, New South Wales, New Zealand Census and Statistical Office, Dr. James Niven, Public Health Commissioners of Government in India, Dr. F. Parkes-Weber, Sir Herbert Read, Dr. J. Robertson, H.M. Treasury, Dr. F. W. Twort, and Dr. Ingram.

The Council would again draw attention to the fact that approved persons interested in medical research are allowed free use of the Library by arrangement with the Librarian, and that assistance is offered to those working on the Council's behalf in the verification of references and in the supply of information as to the scope and general character of particular articles or of recent work in the various branches of medical science.

Eight numbers of the Special Report Series (Nos. 60–7) have been published during the year and three others are in the press. The demand for the earlier Reports is maintained and reprinting has been necessary in some cases, while two (Nos. 19 and 38) are being completely revised, brought up to date, and re-issued. The publication and distribution of the Reports of the Industrial Fatigue Research Board have been added to the duties of the department, and six have been issued during the year (No. 12 and Nos. 14–18) ; four others are in the press.

The publication of *Medical Science* has been continued, and the Council again take the opportunity of expressing their great indebtedness to the following for their assistance in editorial supervision : in Medicine, Dr. J. D. Rolleston ; in Surgery, Professor C. C. Choyce ; in Pathology and Bacteriology, Professor W. Bulloch ; in Neurology, Dr. F. M. R. Walshe ; in Biochemistry, Dr. C. G. L. Wolf ; in Radiology and Electrology, Dr. W. S. Lazarus-Barlow and Dr. Sidney Russ. They desire also to express their appreciation of the services of many other contributors, of whom full lists are published in the index section of each volume.

III. EXPERIMENTAL MEDICINE AND THE RESEARCH WORK OF CLINICAL UNITS.

The policy of the Council in this direction has been fully indicated in previous Reports, and they confine themselves now to a short account of the progress made during the past year.

University College Hospital, London.

(i) *The Council's Department of Clinical Research and the Cardiographic Department of University College Hospital Medical School.* Sir Thomas Lewis, C.B.E., M.D., F.R.S., continues to direct these, working in the whole-time service of the Council and holding the position of Honorary Physician to the Hospital. A whole-time research grant to Dr. A. N. Drury has been maintained, and one has also been made to Dr. R. T. Grant : Dr. C. C. Iliescu of Bukarest, formerly attached to the department, is receiving a whole-time grant for one year's work. During various parts of the year the following have been attached as voluntary workers in the department : Dr. A. M. Wedd of Pittsburg, U.S.A., Dr. Antonio Sebastiani of Rome, Dr. W. N. Horsfall of Sydney, and Dr. W. C. Munly of the United States Army, Portland, Oregon. During the year the accommodation allotted to the department at the Hospital has been expanded and the facilities for work have been correspondingly increased.

The chief work of the department during the year has been a wide investigation of the effects of certain drugs on auricular fibrillation, particularly with a view to ascertaining if the actions of these drugs can be explained on the basis of the theory that fibrillation is due to a ' circus ' movement in the auricle. As a result of the previous researches which were detailed in the last report, and which went far to establish this theory, it became evident that if a drug could be discovered which would produce a notable prolongation of the refractory period of the auricular muscle, there would be a good prospect of arresting fibrillation of the auricles in individual patients. It seemed certain that prolongation of the refractory period would stop the re-entry of the wave, prevent its further circulation and bring it to an abrupt end. The first drug to be investigated from this point of view was atropine, which from previous observations in the laboratory was known to have in some measure the desired effect of prolonging the refractory period. As atropine had often previously been administered during fibrillation of the auricles, and as in the doses used it was not known to affect the auricle, it became necessary to inquire whether it could be used in larger dose without harm. It was found from experiments and from observations on patients that the customary clinical doses are insufficient to produce a maximal heart reaction, and that when adequate larger doses are

given a very definite effect is produced on the fibrillating auricle. To detect and study this reaction a special clinical method of recording was employed. The effect of atropine on the auricle was shown to be in the expected direction, bringing the fibrillating auricle towards, but not actually to, the normal condition of beating.

When the investigations had reached this not unhopeful stage, the discovery of von Frey became known in this country. Von Frey, using purely empirical methods, demonstrated that the alkaloid quinidine is capable of bringing fibrillation of the auricles to an end in many patients. His announcement was considered of so much importance that the observations on atropine were for the moment abandoned; the therapeutic effects of quinidine were first tested and von Frey's statements were soon confirmed. During the clinical observations, new experimental investigations were begun upon the actions of quinidine. The first inquiry naturally sought to discover the effect of quinidine upon the refractory period, for it was expected from the theory of circus movement that this would be its most conspicuous action. This was found to be so. Like atropine, quinidine lengthens the refractory period, and it has this action in conspicuous degree; given in therapeutic doses its action in this respect far surpasses that known in the case of any other drug. This demonstration of the mode of its action thus provided an important confirmation of the main theory. The action of quinidine on the refractory period, moreover, is not its only action on the heart muscle. It has other actions, notably that upon conduction, and this last interferes with the successful treatment of fibrillation in many patients. Another notable effect of quinidine was discovered to be its paralytic effect on the vagus nerves. The more precise nature of this paralytic action was investigated by Dr. H. H. Dale at the National Institute for Medical Research; the alkaloid was found by him to act on the ganglia of the vagus and not upon the vagal endings. In general these experimental investigations have made possible a very complete conception of the action of quinidine in fibrillation of the auricles, and have explained the instances not only of successful, but also of unsuccessful, treatment.

Clinical observations have been undertaken to ascertain the most suitable methods of administering quinidine, its proper dose, the rates of absorption of salts of different solubility, the influence of impurities, the relative potency of allied alkaloids and the influence of simultaneous digitalis therapy, and the like. Attention is also being paid to the after-histories of successfully treated cases: these will be of greater value when they have been traced over a longer period. Attempts are being made to find means of subdividing patients into groups before treatment, according to whether success may be expected or not; some progress has already been made on these lines. Observations on quinidine,

while important from the standpoint of immediate curative treatment, are opening up new problems of a more fundamental kind, and some of these are being pursued.

During the year, the new method of studying the auricle in fibrillation has permitted further investigations of the action of digitalis compounds ; a hitherto unknown action on the auricle has been discovered, and the action on the ventricle has been reinvestigated both clinically and experimentally. An antagonism between digitalis and quinidine has been found and explained, although the effects of digitalis are not sufficient to debar its use simultaneously with quinidine.

These observations on atropine, cinchona alkaloids, and digitalis have formed the basis of articles cited below and also of a series of lectures given by Sir Thomas Lewis at Philadelphia (Hatfield Lectures) and at Portland (Noble Wiley Jones Lectures) during a visit made to America in the present year. Some new observations on the relation of the excitation wave to the axial electrocardiogram were the subject of the Mellon Lecture, delivered at Pittsburg, in which a general conception of potential distribution in the heart was discussed. Sir Thomas Lewis, while in America, received the honorary degree of Doctor of Science from the University of Michigan.

A number of connected observations are in progress upon the action of the vagus upon the heart. A series of apparently paradoxical effects of the vagus on conduction and upon the rate of beating of the ventricle have been discovered : these, although still in large part unexplained, seem to reopen the whole question of the mode of action of this nerve. Some of the results have been published in a preliminary report, and the investigations are being pursued further.

A systematic investigation into the morbid anatomy of some forms of disease of the heart valves has been begun and is now well under way ; new and interesting facts have already come to light.

The study of the after-histories of military patients formerly under observation at Hampstead and Colchester continues. Dr. Grant is now in charge of this work and is assisted by Miss E. Bain. Some sections of this work are near completion, and it is hoped that the first of a series of reports will be completed within the next year.

Sir Thomas Lewis continues to advise the Ministry of Pensions on matters affecting pensioners of the cardio-vascular group.

Publications :—

T. Lewis, A. N. Drury, and C. C. Iliescu—
'Further Observations upon the State of Rapid Re-excitation of the Auricles.' *Heart*, 1921, **8**, 311.
'A Demonstration of Circus Movement in Clinical Flutter of the Auricles.' *Heart*, 1921, **8**, 341.

' A Demonstration of Circus Movement in Clinical Fibrillation of the Auricles.' *Heart*, 1921, **8**, 361.

' Some Observations upon Atropine and Strophanthin.' *Heart*, 1921, **9**, 21.

T. Lewis, A. N. Drury, C. C. Iliescu, and A. M. Wedd—

' Observations relating to the Action of Quinidine upon the Dog's Heart ; with special reference to its Action on Clinical Fibrillation of the Auricles.' *Heart*, 1921, **9**, 55.

A. M. Wedd and W. D. Stroud—

' The Spread of the Excitation Wave related to the Standard Electrocardiogram in the Dog's Heart.' *Heart*, 1921, **9**, 15.

T. Lewis, A. M. Wedd, and C. C. Iliescu—

' The Action of certain Substances upon Auricular Fibrillation.' *Proc. Physiol. Soc., J. Physiol.*, 1922, **56**, vii.

T. Lewis, A. N. Drury, A. M. Wedd, and C. C. Iliescu—

' The Effect of Vagal Stimulation on Intra-auricular Block produced by Pressure or Cooling.' *Proc. Physiol. Soc., J. Physiol.*, 1922, **56**, ix.

' Observations upon the Action of certain Drugs upon Fibrillation of the Auricles.' *Heart*, 1922, **9**, 207.

T. Lewis—

' Post-mortem Notes of a Case of Heart Block.' (In the press.)

T. Lewis (Noble Wiley Jones Lectures)—

3rd lecture. ' The Value of Quinidine in the Cases of Auricular Fibrillation and Methods of Studying the Clinical Reaction.' *Am. J. M. Sc.*, 1922, **163**, 781.

4th lecture. ' The Actions of Atropine and Quinidine in Fibrillation of the Auricles ; Clinical and Experimental Studies.' *Ibid.*, 1922, **164**. 1.

T. Lewis (Hatfield Lecture)—

' The Action of Digitalis in Cases of Auricular Fibrillation and Flutter.' *Ibid.*, 1922, **164**, 157.

T. Lewis (Mellon Lecture)—

' The Interpretation of the Normal Electrocardiogram with Special Reference to the Hypothesis of Limited Potential Differences.' *Arch. Int. Med.*, 1922, **30**, 269.

(ii) *The Medical Unit in the Hospital.* Dr. J. W. McNee, assistant in the unit under the direction of Professor T. R. Elliott, has continued to receive a part-time grant for his work on diseases of the liver and on the metabolism of cholesterin. Part of the work on hepatic disorders has been carried out with the voluntary assistance of Dr. B. Prusik, Lecturer in Medicine in the University of Prague, and an account of it is now almost ready for publication. Dr. McNee has also published the papers mentioned below. He has continued to serve as a member of the Salvarsan Committee.

J. W. McNee—

' The Use of the Van den Bergh Test in the Differentiation of Obstructive from other Types of Jaundice.' *Brit. M. J.*, 1922, **1**, 716.

' On Lipoid Degeneration of the Kidney, and the so-called " Myelin Kidney ".' *J. Path. & Bacteriol.*, 1922, **25**, 425.

' Syphilis of the Stomach.' *Quart. J. Med.*, 1922, **15**, 215.

St. Bartholomew's Hospital.

A part-time grant has been made to Dr. G. K. Stone for the work with Mr. T. P. Dunhill, of the surgical unit in the Hospital, which is referred to later under the heading of Exophthalmic Goitre (p. 68).

The London Hospital.

Dr. A. W. M. Ellis, assistant in the medical unit under the direction of Dr. C. H. Miller, has continued his research work under a part-time grant and with the assistance, provided by the Council, of Miss M. Leeke. He has completed some investigations on the subject of the ' bacteriophage ' phenomenon described by Twort and d'Herelle and will shortly publish the results. With Dr. J. R. Marrack he has also continued his studies of nephritis and is preparing a report on the combined clinical and chemical investigation of a series of cases showing albuminuric retinitis

A part-time grant has also been made to Dr. A. E. Clark-Kennedy for work in the unit. He has continued the work, begun last year with Dr. Ellis, on the action of quinidine in cases of auricular fibrillation and of the comparative merits of quinidine and digitalis in the treatment of the condition (cf. also p. 34). An account of the first twenty cases treated has been published during the year.

A. E. Clark-Kennedy—
' On the Therapeutic Value of Quinidine in the Treatment of Auricular Fibrillation.' *Quart. J. Med.*, 1922, **15**, 279.
A. M. W. Ellis—
' Achylia Gastrica in Addison's Anaemia.' *Guy's Hosp. Rep.*, 1922, **72**, 165.

St. Thomas's Hospital.

The research work on renal disorders and other subjects which has been referred to in previous Reports has been actively continued in the medical unit under the direction of Professor Hugh MacLean. A part-time grant has recently been made to Dr. Isaac Jones, assistant in the unit, while those to Dr. P. C. Brett and Dr. H. Gardiner-Hill have been maintained : a grant has also been made for the expenses of work by Dr. K. Tallerman. The part-time grant for co-operation in this work made to Dr. S. C. Dyke, pathologist to the surgical unit under the direction of Sir Cuthbert Wallace (a member of the Council), has also been continued. The progress of these investigations has hitherto been greatly hampered by the lack of adequate laboratory accommodation, but this difficulty will disappear upon the opening of the new Dunn Laboratory now in construction.

The chief research undertaken during the last year was an investigation into the value of renal tests in genito-urinary surgery, and it is now definitely established that many of the dangers associated with this branch of surgery may be avoided or overcome by a judicious investigation beforehand of the renal efficiency. Indeed, more and more evidence is accumulating that this observation applies to a much wider field of surgery than is perhaps generally recognized A full account of this work will be published by the Council in their Special Report Series.

Investigations of carbohydrate metabolism have also been undertaken, and a new test for liver efficiency has been evolved.

An extensive investigation into the value of basal metabolism in various clinical states has been undertaken with very interesting results. It has been shown that this method of investigation is of value in dealing with various diseases other than those due to thyroid and pituitary damage, and it is hoped that further research here will throw light on some obscure clinical conditions. Dr. MacLean's investigations of cases of kidney disorder dealt with under the Ministry of Pensions at the Cheltenham Terrace clinic, mentioned in previous Reports, continue, and these are yielding information of the first importance for the more accurate prognosis of renal disease.

H. MacLean—
'Our Present Knowledge of the Significance of Albuminuria and Glycosuria.' *West London Med. Journ.*, July, 1921.
'Modern Methods in the Diagnosis and Treatment of Renal Disease.' (Constable & Co.), December, 1921.
'The Prognosis and Treatment of Chronic Renal Disease.' *Brit. M. J.*, 2nd December, 1922.
'Modern Methods in the Diagnosis and Treatment of Glycosuria and Diabetes.' (Constable & Co.), September, 1922.
S. C. Dyke—
'An Inquiry into the more remote Prognosis in War Nephritis.' *Quart. J. Med.*, 1922, **15**, 207.
'A Preliminary Report on some Cases of Contracted Kidney.' *Quart. J. Med.*, 1922, **16**, 1.
'On Isohaemagglutination.' *Brit. J. Exper. Path.*, 1922, **3**, 146.
B. W. Williams and S. C. Dyke—
'Observations on Creatinuria and Glycosuria in Myasthenia gravis.' *Quart. J. Med.*, 1922, **15**, 269.
H. Gardiner Hill—
'An Investigation of the Basal Metabolism in various conditions of certain Endocrine Glands.' *Quart. J. Med.*, 1922, **15**, 331.
J. C. Spence and P. C. Brett—
'The Use of Laevulose as a Test for Hepatic Inefficiency.' *Lancet*, 31st December, 1921.

The Royal Infirmary, Edinburgh.

Part-time research grants have been made to Dr. H. Whitridge Davies and Mr. C. R. Harrington, assistants to Professor J. C. Meakins, in the Department of Therapeutics, University of Edinburgh, and at the Royal Infirmary: Mr. Harrington has now relinquished his grant on receiving an appointment in University College Hospital Medical School, London. With Professor Meakins, Dr. Davies has studied the respiratory function in disease and has made a series of determinations of the basal metabolism in various pathological states. With Professor Meakins and Mr. J. Barcroft (Cambridge) he has investigated the effects of external temperatures on blood volume: the results, which show that increased temperature causes an increase in the volume of the circulating blood, will be published as an appendix to the report of the recent Royal Society Expedition to

Peru. A new apparatus for the quantitative estimation of carbon monoxide in blood has also been devised. Mr. Harrington has investigated the occurrence and distribution of histamine in the human bowel and has completed an investigation into the rate of destruction of histidine in relation to the functional activity of the liver.

J. C. Meakins and H. W. Davies—
'Basal Metabolic Rate: Its Determination and Clinical Significance.' *Edin. M. J.*, 1922, **28**, 4.
H. W. Davies, J. S. Haldane and Peskitt—
'Excretion of Chlorides and Bicarbonates by the Human Kidney.' *Journ. of Physiol.*, 1922, **56**, 269.
H. W. Davies and L. Dautrebande—
'Variations in Respiratory Exchange with Masks of different types.' *Edin. M. J.*, 1922, **29**, 127.
H. W. Davies—
'Methods for Therapeutic Administration of Oxygen.' *Edin. M. J.* (*Trs. Ed. Med. Chir. Soc.*), 1922, **29**, 161.
L. Dautrebande and H. W. Davies—
'A Study of the Chlorine Interchange between Plasma and Corpuscles.' (In the press.)
C. R. Harrington and J. C. Meakins—
'The Relation of Histamine to Intestinal Intoxication. I. The Presence of Histamine in the Human Intestine.' *J. Pharm. & Exper. Therap.*, 1922, **18**, 455.
'The Relation of Histamine to Intestinal Intoxication. II. The Absorption of Histamine from the Intestine.' *Ibid.*, 1922, **20**, 45.

Research Work in Professional Practice.

As mentioned in earlier Reports, it has always been the Council's policy to utilize the opportunities of medical men for research work in clinical medicine arising from their hospital or private practice. Under this heading may be mentioned the work of Dr. H. J. Starling (p. 67) at Norwich, Dr. E. E. Laslett (p. 68) at Hull, Dr. Ivy Mackenzie (p. 67) and Dr. D. K. Adams (p. 71) at Glasgow, Dr. W. E. Hume and Miss M. Kirkhouse (p. 94) at Newcastle, and Dr. L. S. T. Burrell (p. 77), Dr. Geoffrey Bourne (p. 83) and Dr. P. Hamill (p. 83) in London. These researches will be mentioned again under the appropriate subject headings in Section V on the pages indicated.

The St. Andrews Institute of Clinical Research.

In former Reports the Council have referred to their interest in the important schemes of research being pursued under the direction of Sir James Mackenzie at the St. Andrews Institute of Clinical Research. During the past year they were glad to find themselves able to increase the financial support given to the work of the Institute, after full consultation with Sir James Mackenzie. The personal grant formerly made to Dr. A. Rowand for work at the Institute on the early signs of tubercular disease in children has been continued. In addition, a grant has been made towards the annual cost of maintaining the system of

records which forms a fundamental part of the general scheme of research. Honoraria have also been offered by the Council to Professor P. T. Herring and Professor David Waterston, University of St. Andrews, in respect of the special services which they are able to render by bringing investigations in their laboratories into the most effective relation to the observational work within the Institute.

IV. THE DETERMINATION OF BIOLOGICAL STANDARDS AND THE METHODS OF BIOLOGICAL ASSAY AND MEASUREMENT.

The Council continue to give prominence among their schemes of research work to a group of investigations which have for their main object the improvement of the quantitative or qualitative accuracy which it may be possible to attain in various branches of medical science. The considerations upon which the Council's policy is based have been discussed in some detail in previous Reports.

One of the main directions of work is in the determination of methods of assay for substances of which the physiological effects cannot be quantitatively estimated by direct chemical means: these include antitoxins and sera, glandular extracts and certain drugs. Another branch of work is the standardization of pathological methods with a view to uniformity of results: this includes both the maintenance of central sources for the supply of standard types of micro-organisms and of standard sera, and the devising of serological and other methods for general acceptance. To these groups may here be added the study of anthropometric methods and standards of the medical measurement, structural and functional, of the human body.

Work on Biological Standards at the National Institute for Medical Research.

Standard Tests for Arsenobenzol Compounds.

The routine biological control of salvarsan products for toxicity has been continued by Miss F. M. Durham and Miss J. Marchal, under the direction of Dr. H. H. Dale, licences being issued by the Council on behalf of the Board of Trade, as in former years. A problem of a new kind, however, was presented by the reports reaching the Council from several sources, to the effect that Neosalvarsan of British manufacture was gravely defective in therapeutic properties. An investigation of its curative effect on an infection of mice with *Trypanosoma equiperdum* confirmed this suggestion. This method of testing, introduced by American workers, had not, however, been brought into direct experimental relationship with the therapeutic action of these preparations on syphilis in man. A combined investigation was therefore undertaken, a series of batches being tested independently by the department for their curative action on the trypanosome infection in mice, and by Major C. F. White and Mr. C. H. Mills at the Military Hospital, Rochester Row, for their curative effects in selected cases of syphilis of a uniform type, with lesions readily accessible to microscopic investigation. The results of the two

investigations showed a correspondence so clear and accurate that the test on trypanosomiasis in mice could be adopted without hesitation as an index of therapeutic value in human syphilis. As a result, the manufacturers have been able to modify their processes so as to produce Neo-salvarsans which satisfy the tests now imposed, both for freedom from undue toxicity and for satisfactory therapeutic potency. This investigation has formed the subject of a report published jointly by Dr. Dale, Dr. Burn, Miss Durham, Miss Marchal, Major White, and Mr. Mills (p. 19).

Standardization of Pituitary Extract.

Mention has been made above (p. 18) of Dr. Dudley's investigations of the extract of the posterior lobe of the pituitary body. This extract has in the past decade been very widely used, especially in obstetrics, on account of its potent stimulant action on the plain muscle of the uterus. The chemical nature of its active principles being unknown, and apparently beyond the reach of the available methods of investigation, it is essential to have an efficient biological method of adjusting its strength to a recognized standard. Attempts to effect such an adjustment have been made for many years past, and a method has even been incorporated in the last edition of the United States Pharmacopoeia. That the methods used, however, have been imperfect, or variable in their application, is made abundantly evident by an investigation carried out by Dr. Dale and Dr. Burn, who found that samples of this product obtained from five different makers who supply it in this country, were so widely different in their potency, that the strongest was no less than eighty times as powerful as the weakest in its action on the muscle of the uterus. Such variation in the action of a preparation which is essentially a remedy for emergencies, capable of saving life if given in suitable dosage, of failing to save if too weak, and of introducing a new and serious danger if too strong, is clearly a matter of the gravest public importance. In a report which has been published (p. 19), Dr. Dale and Dr. Burn indicate a method of producing a trustworthy standard of reference, and give details of a method of comparison which, if faithfully observed, should suffice to eliminate any significant fluctuations in the activity of this extremely valuable, but dangerously powerful remedy.

Standardization of Anti-Diphtheritic Serum.

Dr. Colebrook, having been transferred for the time being to Sir Almroth Wright's department at St. Mary's Hospital, has been obliged to relinquish the work which he had begun on the preparation of British Standards for Diphtheria and Tetanus Antitoxic Sera. The Council have been fortunate in securing the services of Dr. P. Hartley, who will bring a long and varied experience of similar problems to the completion of this important

piece of national service. Several batches of diphtheria toxin have been prepared, and are being matured and evaluated with the special accuracy needed for their use in the fixation of an antitoxin standard. The drying of serum without impairing the solubility of its constituents is a difficulty which has for many years been encountered in serological laboratories. It has special importance for the preparation of the perfectly dried sample of antidiphtheritic serum which is contemplated as the standard of antitoxin for this country. The problem is in sight of satisfactory solution, and this first serum standard for Britain should be ready for issue in the early future. Advantage will be taken of the recent international agreement on the unit of diphtheria antitoxin, to ensure exact conformity of the British unit to the accepted International Standard.

Other Investigations.

Mention is made elsewhere in this Report (p. 77) of the inquiry into Tuberculin, participation in which has formed part of Captain Douglas's work at the Institute.

Reference has already been made to Mr. Barnard's studies of optical and other technical methods (p. 27).

The National Collection of Type Cultures.

By the courtesy of the Governing Body of the Lister Institute the Collection has continued to be housed at the Institute. Dr. J. C. G. Ledingham of the Institute staff has continued to act as Director on the Council's behalf. Dr. R. St. John-Brooks and Miss M. Rhodes, in the whole-time service of the Council, are Curator and Assistant Curator respectively.

During the year under review the work of the Collection, with regard both to the number of types received and the number of cultures issued to correspondents, has made steady progress. Over three hundred fresh types were received into the Collection and over two thousand five hundred cultures were distributed. Early in the year the catalogue of the National Collection was published by the Council, and it is hoped that this will be valuable to microbiologists at home and abroad.

The working relations established with the British Mycological Society, mentioned in the last Report, have had good results, and a small but representative collection of fungi of importance in plant pathology is now housed in the National Collection. It is hoped that mycologists will make the fullest use of the material available.

During the year many valuable additions were again made to the Collection. These included :

Mesentericus types from 'ropy' bread isolated by Miss Jordan Lloyd.
Diphtheria and Diphtheroid organisms presented by the Wellcome Institute for Physiological Research and by Major Gordon Bell, R.A.M.C.

A collection of haemolytic and non-haemolytic *B. coli* organisms from Professor Leonard Dudgeon, St. Thomas's Hospital, and a strain of *B. coli* showing ' bacteriophage ' from M. Gratia.

Organisms isolated from cases of sprue presented by Dr. J. T. Duncan, London School of Tropical Medicine.

Collections of plant fungi presented by Mrs. N. L. Alcock, Ministry of Agriculture, Harpenden ; Dr. E. J. Butler, Imperial Bureau of Mycology, Kew ; Dr. W. J. Dowson, R.H.S. Gardens, Wisely ; Mr. S. P. Wiltshire, Long Ashton Experiment Station, Bristol ; Dr. G. H. Pethybridge, Department of Agriculture, Dublin ; and others.

Soil organisms from Dr. A. Thaysen, R.N. Cordite Factory, Holton Heath ; and a collection of moulds isolated from food in cold storage and from diseased tomatoes presented by Mr. F. T. Brooks, Botany School, Cambridge.

A collection of organisms isolated from tan liquors presented by Mr. R. Leslie Collett, F.I.C., British Leather Research Association.

Organisms isolated from mouse epizootics by Dr. W. W. C. Topley, Charing Cross Hospital Medical School.

A collection of Aspergilli pathogenic to birds, and various animal Pasteurellas from Dr. Nathaniel Lucas, R.Z.S. Gardens, Regent's Park.

Monilia species from Professor Aldo Castellani.

Bacteria causing diseases of tobacco plants and of citrus fruits from Miss E. M. Doidge, Botany Department, Pretoria, South Africa.

Meningococcus types from Dr.M. H. Gordon, St. Bartholomew's Hospital.

Cultures of *Bacillus acidophilus* from Dr. L. F. Rettger, Yale University, U.S.A., and from Dr. Coulthard, Glasgow.

Pneumococcus types from Dr. F. Griffiths, Ministry of Health Laboratories.

Strains of *Actinomyces bovis* (Wolff-Isreal) from Professor Mackie, University of Cape Town.

Leishmania donovani, *L. tropica*, *L. canis*, and *Leptomonas du Gecko* from Professor Nicolle, Institut Pasteur de Tunis.

For all these the Council desire to express their grateful acknowledgements.

During the year the hospitality of the laboratory was at different times extended to Dr. Toda of the Nippon Yusen Kaisha Medical Service and to Mr. S. T. Mitchell, M.R.C.V.S., Veterinary Research Department of the Union of South Africa.

The work of propagating certain pathogenic organisms is not without danger, and the Council have to record with great regret that in carrying on a strain of *B. tularense* not only the Curator and Assistant Curator but also a member of the staff of the Lister Institute, Dr. Schütz, have fallen victims to infection by this organism—an accident which seems, according to American experience, to befall practically all laboratory workers who attempt the cultivation. The illness produced, known as ' tularaemia ', is an unknown one in this country, and is of a protracted nature although scarcely ever fatal in man. The Council have heard with pleasure that recovery has taken place in all three cases mentioned. It has been deemed inadvisable to continue the propagation of this dangerous organism in the National Collection.

' Catalogue of the National Collection of Type Cultures.' *M. R. C. Special Report Series*, No. 64, 1922.

Production of Standard Cultures and Sera.

Enteric and Dysenteric Infections.

The work of the Standards Laboratory at Oxford under Professor Dreyer's general direction has been maintained as in former years by Dr. A. D. Gardner, in the whole-time service of the Council, with the assistance of Miss E. F. Stubington.

The Laboratory has continued to supply to all approved applicants standard agglutinable cultures and standardized agglutinating sera made with the following eleven varieties of bacilli: *B. typhosus*; *B. paratyphosus* A; *B. paratyphosus* B; *B. enteritidis* (Gaertner); *B. aertrycke* (Mutton); *B. dysenteriae* (Shiga); and five varieties of *B. dysenteriae* (Flexner), viz. 'V', 'W', 'X', 'Y', and 'Z'. A polyvalent agglutinating serum for the five 'Flexner' bacilli has also been supplied. The Laboratory has also provided a number of workers with permanent formalized gelatin tubes showing 'standard agglutination' for both the enteric and dysenteric types of cultures.

During the course of twelve months 297 orders for cultures and 116 orders for sera have been executed, and the following total quantities have been issued: standard cultures, 32,365 test-portions (97,095 c.c.); standard sera, 28,970 test-portions (2,897 c.c.). These figures are somewhat higher than those for the previous twelve months. An analysis of the orders shows that 143 were received from bacteriologists working in Hospital or University laboratories, 53 from public health officers, 41 from colonial and foreign workers, 40 from military and naval laboratories, and 20 from private laboratories or practitioners.

Owing to the receipt of a number of orders for standard cultures of bacilli of the 'intestinal' group other than those already issued, it is proposed in future to issue standard cultures and sera made with *B. paratyphosus* C, *V. cholerae*, and *B. aertrycke* (Newport), in addition to those already available.

The production of standardized cultures has hitherto been accompanied by an undesirable amount of wastage, due mainly to two causes, namely contamination with moulds, and the uncontrollable variability of the agglutinative properties of the bacilli. After a great deal of investigation, the former difficulty was traced to the influence of a mould-infected cold-store, and a simple alteration of the storage system has almost entirely eliminated this trouble. The second difficulty has been largely overcome by means of a process of colony-selection, by which it is possible in the great majority of cases to ensure the production of standard cultures of good quality.

The staff of the Laboratory are constantly engaged in experimental work of various kinds. Dr. Gardner has completed two series of experiments—one upon the agglutination of the five types of Flexner bacilli by normal human sera, and the other series upon the serological stabilities of the same five types of bacilli. He

has also been collaborating with Dr. Ainley Walker in research on the variability of bacteria.

Finally, the staff of the Laboratory have extended their range of work by undertaking the standardization of antigens for the Dreyer-Ward 'Sigma' reaction (see below) on behalf of serologists who are using this test.

A. D. Gardner—
'The Normal Limit of Agglutination for *B. dysenteriae* (Flexner) and the Sensitiveness of Suspensions.' *Lancet*, 17th December, 1921.

International Serological Standards.

The Council have been glad to co-operate in a scheme of work in this subject inaugurated by the Health Committee of the League of Nations, as already mentioned on p. 10. The questions involved were discussed at an international conference convened in London in December, 1921, at the instance of the Health Committee. It was then agreed that an endeavour should be made to establish international standards for sera and for serological methods, and the different countries represented were asked to undertake various subjects of research with this end in view. The subjects undertaken in Great Britain were (*a*) the standardization of methods for the sero-diagnosis of syphilis : (*b*) the standardization of anti-dysenteric sera ; and (*c*) the standardization of anti-pneumococcic and anti-meningococcic sera. A further conference has recently been held in Paris to review the progress of the work.

The Sero-diagnosis of Syphilis.

Reference was made last year to the 'Sigma' test for syphilis devised by Professor Georges Dreyer and Dr. H. K. Ward (p. 78), for which quantitative accuracy was claimed. Before the inception of the international scheme just mentioned, the Council had arranged for a comparative trial of the 'Sigma' and the Wassermann reactions. A thousand specimens of blood from syphilitic patients and from controls were submitted to examination by each method independently, the clinical records of the cases being unknown to the pathologists until after their results had been communicated. Five hundred specimens were collected at the London Hospital by Dr. J. R. C. Stephens, under the direction of Dr. J. H. Sequeira, and were submitted to the Wassermann test by Dr. P. Fildes and Dr. G. T. Western ; the other five hundred were obtained by Dr. R. O. Swain at the Middlesex Hospital and were similarly tested there by Professor J. McIntosh and Dr. A. N. Kingsbury. Duplicates of all the specimens were at the same time examined at the University of Oxford by Professor Dreyer and Dr. Ward, using their 'Sigma' reaction. The results of this trial will shortly be ready for publication, with those of similar trials spontaneously carried out at the Royal

Victoria Hospital, Belfast, by Dr. T. Houston and his colleagues, and at Trinity College, Dublin, by Professor Adrian Stokes.

After the international conference last year, another comprehensive series of tests was arranged in which the blood from each case is being examined not only by the Wassermann and 'Sigma' tests, but also by two other methods, the Sachs-Georgi and Meinicke III, the tests by all four methods being made in this series by one and the same observer. The direction of this work was undertaken by Colonel L. W. Harrison, by whom all necessary arrangements were made at St. Thomas's Hospital, London; the tests themselves are being made by Dr. E. J. Wyler, working at the Hospital in the whole-time service of the Council. The Council have provided the necessary expenses and assistance. The investigation is still in progress.

Dr. W. D. O'Kelly of University College, Dublin, has communicated to the Council the results of a comparison of the Wassermann test as performed by different observers with variations in technique. He has now relinquished the part-time grant formerly made for this and other work.

E. J. Wyler—
'Further Observations on the Wassermann Test with Prolonged Fixation at Ice-chest Temperature.' *J. Path. & Bacteriol.*, 1922, 25, 271.

Anti-Dysenteric Serum.

The direction of investigations into this subject has been entrusted to a Sub-Committee under the chairmanship of Captain S. R. Douglas, Director of the Council's Department of Experimental Pathology. Work undertaken for the Sub-Committee by Dr. R. A. O'Brien at the Wellcome Research Laboratories is at present in progress.

Anti-pneumococcic and Anti-meningococcic Sera.

The similar Sub-Committee appointed for this subject is presided over by Dr. M. H. Gordon. Work on the types of pneumococci and the production of anti-pneumococcic serum is being carried out by Dr. F. Griffith of the Ministry of Health, and the work of Professor E. E. Glynn and Miss L. Digby, mentioned elsewhere (p. 83), is also within the scope of the Sub-Committee.

Progress in the proposed work on anti-meningococcic serum has been retarded owing to the scarcity of material at the present time due to the small number of cases occurring in the country. A working arrangement has been made with the Ministry of Health for the utilization of such opportunities as may arise. In the meantime Dr. E. G. D. Murray continues, at the University of Cambridge, his whole-time work for the Council to which reference has been made in previous Reports.

Anthropometric Methods and Standards of Medical Measurement.

Under the general direction of Professor Dreyer, Dr. F. G. Hobson has continued his work at the University of Oxford, for which the Council are making a whole-time grant. As mentioned in previous Reports, the main object of this investigation has been the correlation of Professor Dreyer's 'vital capacity' test for physical fitness with other measurements. The calculation and analysis of the data already collected has been continued, and certain aspects of the measurements which had not previously been considered in detail are now under special study. A preliminary report has been submitted to the Committee on Anthropometric Methods (p. 115), under the Chairmanship of Sir Arthur Keith, and is now being examined in the Council's Statistical Department. Some other lines of investigation have also been begun, notably the study of basal metabolism in relation to other measurable physical characteristics, and the examination of pulse-rate, blood-pressure, haemoglobin content, and the factors that may influence these.

At Guy's Hospital, London, Dr. G. H. Hunt and Professor M. S. Pembrey have extended their observations upon the influence of muscular work upon the heart, especially in relation to the factors that influence the pulse ratio. Comparative observations have been made upon the pulse ratio as a test for physical fitness in trained, untrained, and unfit subjects doing various amounts of work. In addition, a long series of comparative observations upon the vital capacity, pulse ratio, blood-pressure, and mercury manometer test have been made in relation to the stem length and weight of the subjects. The Council have defrayed the special expenses of the investigation.

At the University of Manchester and at the Manchester Grammar School, Dr. A. A. Mumford has continued his observations of the 'vital capacity' test. Dr. Lucy Cripps, in the whole-time service of the Council at the National Institute, has also been engaged in work upon tests for physical efficiency, particularly in women, while the data collected in the Royal Air Force by Wing-Commander Martin Flack have been made available for the purposes of the Committee. Reference is made elsewhere (p. 77) to Dr. Burrell's application of the 'vital capacity' test to the diagnosis of pulmonary tuberculosis in man.

V. RESEARCH IN SPECIFIC SUBJECTS.

Problems of Child Life.

Pre-Natal Studies.

The Factors contributing to Dead Births and Premature Births.

The present year has seen the end of the first phase of this investigation, during which the workers named below have been principally engaged in the systematic examination of cases of dead birth and premature birth. A large number of cases having now been examined, the combined results have been placed in the hands of a special sub-committee consisting of Dr. J. W. Ballantyne, Dr. J. S. Fairbairn, and Mr. Eardley Holland, from whom a report is shortly expected for publication by the Council. On the recommendation of the sub-committee further work is in the meantime to be restricted to special problems which have arisen during the more general phase of the inquiry: at the same time, systematic examinations of cases of neo-natal deaths, especially of deaths during the first two weeks of life, are to be made.

During the past twelve months Dr. Francis J. Browne, working at the Royal Maternity Hospital, Edinburgh, in the whole-time service of the Council, has continued his investigation of the causation and pathology of still-births. He has now made 570 post-mortem examinations of cases of still-birth and early neo-natal death and is engaged in working up the details of a second series of 200 cases uniformly with the series already published. He is also beginning new lines of work, especially in the experimental investigation of problems in ante-natal pathology.

At the Glasgow Maternity Hospital Dr. J. N. Cruickshank, with a half-time grant from the Council, has continued Dr. A. M. Kennedy's former work. Part-time grants have also been made here to Dr. J. Hewitt and to Dr. M. J. Miller. At this centre, post-mortem examinations have now been made of 940 still-born and live-born infants, while Dr. Kennedy's previous study of 200 mature foetuses has been continued by a series of 200 premature infants examined by Dr. Cruickshank. The rôle of syphilis has been further investigated, and this formed the subject of a preliminary paper read by Dr. Cruickshank before the British Medical Association in July last. Dr. Miller has been making a special study of the weights of various organs in relation to body weight, based on the records of 1,000 cases. Dr. Hewitt has been studying chronic inflammations of the uterus, and is now collecting the results of various methods of treating pyelitis during pregnancy. Pathological material has also been collected and prepared here for Miss Hewer's work at the London School of Medicine for Women on the histology of the ductless glands and other organs in cases of prematurity, still-birth, and neo-natal death.

Dr. N. B. Capon, formerly in receipt of a grant for work of this kind at the University of Liverpool, has published his results.

At the King Edward VII Hospital, Cardiff, Dr. G. I. Strachan has continued to receive a part-time grant for work in this subject under the general direction of Dr. H. A. Scholberg, and has paid special attention to placental abnormalities.

In London Dr. A. C. Palmer, working at the London Hospital under the direction of Professor H. M. Turnbull, and Mr. L. G. Phillips, working at Queen Charlotte's and St. Mary's Hospitals under the direction of Dr. E. H. Kettle, have continued under this scheme to receive part-time grants.

Some expenses for work on the subject have also been allowed to Dr. Clara Stewart (Mrs. M. J. Stewart), University of Leeds.

J. W. Ballantyne, E. Holland, F. J. Browne, J. N. Cruickshank, G. I. Strachan and others—
'Discussion on Still-births and Neonatal Deaths.' *Brit. M. J.*, 30th September, 1922.
F. J. Browne—
'Pneumonia neonatorum.' *Brit. M. J.*, 25th March, 1922.
F. J. Browne and J. W. Ballantyne—
'The Problems of Foetal Post-maturity and Prolongation of Pregnancy.' *Journ. of Obst. and Gynec. Brit. Empire*, 1922, **29**, 177.
F. J. Browne and J. Miller—
'Extra-Genital Chorion-Epithelioma of Congenital Origin.' *Ibid.*, 1922, **29**, 48.
N. B. Capon—
'General Oedema of the Foetus.' *Ibid.*, 1922, **29**, 239.
J. N. Cruickshank—
'Persistent Cloaca with Imperforate Anus as a Cause of Foetal Ascites.' *Brit. M. J.*, 10th December, 1921.
'Syphilis as a Cause of Ante-Natal Death.' *Ibid.*, 30th September, 1922.
T. Hewitt—
'Chronic Metritis.' *Trans. Roy. Medico-Chirurgical Soc. of Glasgow*, 1922, **16**, 171.

The Toxaemias of Pregnancy.

With a half-time grant from the Council, Dr. O. L. V. de Wesselow has continued his work at St. Thomas's Hospital, London. He has investigated the toxaemias of pregnancy from a chemical standpoint. Examination of the kidney functions appears to give information as to the course of the disease, which is of value to the clinician in determining whether induction of labour is necessary or desirable. Attempts to obtain evidence of any liver deficiency by estimations of the plasma fibrinogen and lipase, and by determinations of the urinary nitrogen distribution, led to no conclusive results. An examination of the calcium and inorganic phosphorus content of the blood in pregnancy showed that no notable variations from the normal occur. The inorganic phosphorus of the blood plasma was found to be at a high level during lactation. Dr. de Wesselow also continues to act as Secretary to the London Child Life Committee (p. 112).

A part-time grant has recently been made to Dr. A. Fitch for

work in this subject under the direction of Professor J. M. Beattie at the University of Liverpool.

At the close of the period under review the Council were glad to join the Obstetrical and Gynaecological Section of the Royal Society of Medicine in the appointment of a Committee to investigate the Prognosis and Treatment of Eclampsia. The constitution of the Committee is given in the Appendix (p. 117). A grant for the expenses of the work has been made.

O. L. V. de Wesselow—
'Some Chemical Observations on the Toxaemias of Pregnancy.' *Journ. of Obst. and Gynec. Brit. Empire*, 1922, **29**, 21.
'The Calcium and Inorganic Phosphorus Content of the Maternal Blood during Pregnancy and Lactation.' *Lancet*, 29th July, 1922.
O. L. V. de Wesselow and J. M. Wyatt—
'Chemical Observations on the Toxaemias of Pregnancy.' *Proc. Roy. Soc. Med.* (Sect. Obst. & Gynec.), 1922, **15**, 57.

Metabolism and General Physiology in Pregnancy and the Lying-in Period.

At the Royal Free Hospital and School of Medicine for Women, London, Lady Barrett and Professor Winifred Cullis have continued to direct work on behalf of the Council. The whole-time grant to Mrs. C. P. Williams, and the part-time grants to Miss M. Bond, Miss E. Hewer, and Miss S. Widdows have been continued. Dr. Williams has been making chemical analyses of the blood plasma of pregnant women, the immediate object being the determination of a standard for normal cases. Miss Widdows has been investigating the calcium content of the blood in pregnant and normal women. Miss Hewer's work has already been mentioned (p. 49).

Winifred C. Cullis, E. M. Oppenheimer and M. Ross-Johnson—
'Observations on Temperature and other Changes in Women during the Menstrual Cycle.' *Lancet*, 4th November, 1922.
M. Bond—
'A Modification of Basal Diet for Rat Feeding Experiments.' *Bio-Chem. J.*, 1922, **16**, 479.

Influence of Maternal Nutrition upon the Infant.

An inquiry has been begun at St. Thomas's Hospital, London, under the direction of Dr. J. S. Fairbairn, a member of the London Child Life Committee. A whole-time grant for the collection of the necessary data has been made to Miss Bruce Murray.

Post-Natal Studies.

The Influence of Various Factors on Nutrition and Growth.

The inquiry under the auspices of the Scottish Child Life Committee (p. 113) has been continued, both by the collection of records from Child Welfare Centres and by the home visitations

of special workers in the service of the Council. Miss A. M. T. Tully and Miss E. Urie in Glasgow, Miss J. Swanson (under the direction of Dr. T. Y. Finlay) in Edinburgh, and Miss M. L. Clark in Dundee, are taking part in the work, while Miss M. R. Gribbon also did so until the beginning of the present year. Miss Jean Agnew, Secretary to the Committee and in the service of the Council, has also taken part in the work.

Records have been made upon specially prepared schedules at the various Child Welfare Centres in Glasgow, Edinburgh, and Dundee. As was expected, the accuracy and fullness of detail of these records vary widely, and a scrutiny of the material already collected has led to a thorough weeding out of imperfect records. The results suggest the advisability of repeating the analysis when a much larger number of records has been collected, and it is accordingly proposed to do this. The attempt to obtain information at these Centres, in spite of the cordial efforts to help made by the various officials, has been in great measure disappointing. It was expected to find that serious attempts were being made towards gaining much-needed information about the factors which actually modify the condition and development of children, but in the planning of the work of these Centres these possibilities of gain seem to have been left out of account and the workers have not been trained to keep accurate records. The congested state of the Centres, moreover, makes it extremely difficult for even a trained worker to take good records. It is satisfactory, however, that over 3,000 schedules, having over 5,000 height and weight records, have already been completed with sufficient accuracy. The results up to date have been tabulated and correlated by Miss Agnew, Miss Clark, and Miss Swanson, and the work is still in progress. The state of the child during the first year, to which the records of Child Welfare Centres apply, is probably closely related to prenatal conditions : environment, so to speak, has not yet had time to tell directly upon it. The number of inmates per room, the size of the family, and the position of the child in the family, if these have any relationship to the condition of the child, may have acted prenatally, while the health of the mother during pregnancy must have acted in this way. On the other hand, the feeding of the infant must have a direct effect.

From an analysis of the comparatively small number of figures now available no correlation is manifest between the nutrition of the child under one year and the size of the family, position of the child in the family, or number of persons per room. The suggestion is that irrespective of these conditions, even if unfavourable, the infant may still start life unhandicapped. On the other hand, there appears to be an indication of a direct correlation between the condition of the child and the health of the mother during pregnancy. As regards the influence of feeding, the information obtainable is not sufficient to allow

a valid estimate to be made of the effect of this important factor, because the data are not quantitative. All that could be done was to attempt to determine whether any differences in growth and nutrition could be found as between infants breast-fed for three months and over and those not breast-fed at all, or breast-fed only for a shorter period than three months. No correlation, however, could be established here.

In Edinburgh Dr. T. Y. Finlay has continued his investigation into the effects of various forms of feeding. He has now accumulated a large series of records of the feeding of infants in Edinburgh, and hopes to follow the development of these children during the early years of life, in order to estimate, if possible, the effects of early feeding on development, resistance to disease, and the like.

During the year home visiting has been continued by the workers already named, and Miss Tully has been working on the records previously collected. By February 1921 the records of over 500 families visited in Glasgow, and of 220 in Dundee, had been accumulated, and of these a preliminary survey was made in order to see where the work was leading and what modification of methods, if any, was desirable. This involved an investigation of the best methods of expressing numerically the state of growth and nutrition, and, after a study of the previous work upon the subject and the analysis of figures specially collected, it was decided to take height in inches as the measure of growth and height for age as the measure of nutrition. The possible effect of race on the stature and nutrition of the children had also to be investigated. Miss Tully, with the co-operation of Dr. Weir and other members of the Anatomical Staff of the University of Glasgow, obtained records of about 4,000 school children, thanks to the permission readily and courteously granted by the Glasgow Education Authority to visit and examine the children of certain of the elementary schools, and to the sympathetic and efficient help given by the head masters of these schools in making the necessary arrangements. An examination of the records showed that over 91 per cent. of the children were of the brown-haired or completely mixed type, and that no notable difference in stature subsisted between the fair-haired and dark-haired groups. In Glasgow it appears that the population is racially homogeneous and that the stature and nutrition are not affected by race. It has already been shown by Galton, Karl Pearson, and Davenport that the size of the offspring is related to the size of the parents. The high proportion of stunted adults in Dundee gave an opportunity of investigating this, and the results obtained confirmed the findings of these previous investigators. The investigation of 4,000 school children also gave material for determining the possible effects of recent illness upon the nutrition of the children, but no correlation could be found. In investigating the influence of the size of the family, the family income, and the air space per person, instead of dealing with comparatively small numbers of children

at each age, a loaded average of all ages was taken. From this there seemed to be a direct correlation between these factors and the nutrition of the children.

The figures have been submitted to the Statistical Department of the Council, and a preliminary report, while indicating that an extension of the investigation is necessary if decisive conclusions are to be drawn, generally supports the findings here summarized.

Jean Agnew—
'Mortality Rates in Glasgow Families: An Analysis of the Various Kinds of Wastage of Child Life in Well-to-do and in Poor Families of Varying Size.' *Glas. M. J.*, 1922, **98**, 145.
Madge R. Gribbon—
'Some Factors Modifying the Nutrition of Children; a Survey of 3,000 of the Most Marked Cases of Malnutrition in Viennese Children, made in the Summer of 1921.' *Edin. M. J.*, 1922, **29**, 12.

Metabolism in Infants.

At the Royal Hospital for Sick Children, Glasgow, Dr. G. B. Fleming has made a comparison of the basal metabolism in cretinism and mongolian idiocy respectively, and he has examined the respiratory exchanges in cases of congenital biliary atresia. He hopes in the coming winter to begin an investigation of the effect of ultra-violet rays on metabolism in rickets. The Council have made a grant towards his expenses.

The part-time grant to Dr. J. A. Gardner for work at St. George's Hospital, London, has been continued. He has done further work on cholesterol metabolism, particularly in the early months of life, on the lines mentioned in previous reports. In addition to the publications quoted below he has at present in preparation further papers on the sterol content of cow's milk, on the sterol metabolism of infants, and on the autolysis of the suprarenal gland.

Geoffrey B. Fleming—
'The Practical Application of the Determination of the Respiratory Exchange in Health and Disease.' *Glas. M. J.*, 1921, **96**, 337.
'Respiratory Exchange in Biliary Atresia.' *Am. J. Dis. Child.*, 1922, **23**, 66.
'The Respiratory Exchange in Cretinism and Mongolian Idiocy.' *Quart. J. Med.*, 1922, **16**, 11.
J. A. Gardner and F. W. Fox—
'On the Origin and Destiny of Cholesterol in the Animal Organisms. Part XII. On the Excretion of Sterols in Man.' *Proc. Roy. Soc.*, B., 1921, **92**, 358.
'Origin and Destiny of Cholesterol in the Animal Organism. Part XIII. On the Autolysins of Liver and Spleen.' *Ibid.*, B., 1922, **93**.

Rickets.

At the Institute of Physiology, University of Glasgow, Professor D. Noël Paton (a member of the Council) and Dr. A. Watson have continued their studies of experimental rickets, for which

the Council provide special expenses and the part-time assistance of Mr. A. P. Orr. The whole-time grant to Dr. S. V. Telfer has also been maintained, and a part-time grant for a few months' work has been made to Mr. J. S. Sharpe.

Further experiments have been carried out by Professor Noël Paton and Dr. Watson to test the possibility that rickets may be an infectious disease, and to elucidate the modes in which dietetic modifications may cause or prevent the disorder.

Dr. Telfer has continued his studies of the exchanges of calcium and phosphorus begun during the previous year and the results are appearing in the *Quarterly Journal of Medicine*. The effects of calcium in the diet on the excretion of fats and phosphorus have been investigated, both in infants and in animals. The retention and use of the bone-forming elements in a series of normal and rachitic infants have also been determined. With Professor Noël Paton, the effects of the calcium content of the diet on the storage of calcium in the skeleton have been studied in dogs. Observations upon the part played by the mineral elements of diets in children have been supplemented by experiments upon pups, and the effects produced upon the skeleton have been determined by analyses of the bones. Further work is being done to find the conditions governing the absorption of the bone-forming elements, and the influence of fats upon this absorption.

With the object of ascertaining the source of the guanidine in *tetania parathyreopriva* with a view to gaining better knowledge of the causes of tetany in rickety children, Mr. Orr has been investigating the guanidine content of the blood and liver in dogs after parathyreoidectomy. The isolation of the guanidine from the liver has proved most difficult, and fresh methods have had to be devised and tested. Mr. Sharpe has been following up the evidence, as adduced by Reisser and further supported by Shanks, that choline may be a precursor of guanidine, and he has investigated the choline content of the blood in normal and in parathyreoidectomized dogs. For this he has devised a chemical method depending upon the fixation of the choline by iodine, and he has used the biological method of Dale. The suggestion has been advanced that the convulsions of eclampsia in pregnant women are of the same nature as tetany, and Mr. Orr has investigated the guanidine content of the blood in cases of this kind at the Royal Maternity Hospital, Glasgow. He has been so far unable to detect any increase in the guanidine content of the blood.

The grant for the expenses of the clinical investigation of rickets, under the direction of Dr. Leonard Findlay at the Royal Hospital for Sick Children, Glasgow, has been maintained, and a part-time grant has been made to Dr. J. B. D. Galbraith for assistance in the work. Dr. Galbraith has studied, during winter and summer, the results of different therapeutic measures in

47 cases of rickets, and an account of this work will be published in due course. He has examined the osseous development in over 80 children from soon after birth throughout the first 12 to 18 months of life with special reference to the nature of the diet.

Major H. S. Hutchison has, since his return to Glasgow from India at the end of 1921, been extending his previous work on fat absorption in infantile atrophy and checking the results by observations with the bomb calorimeter. The Council are making a part-time grant.

Dr. Grace Anderson, at the Royal Hospital for Sick Children and at the University of Glasgow, has worked in the whole-time service of the Council upon the estimation of the calcium and phosphorus content of the whole blood and the distribution of calcium in the bloods of normal and rachitic children. Estimations of the ratios of the total calcium to total phosphorus, and of the total calcium to inorganic phosphorus of the blood in normal and in rachitic children, have been made. She is investigating further the inorganic phosphorus of the serum with special reference to its possible seasonal variations and to its diminution in rickets.

Professor Edward Mellanby, whose work will be mentioned again below under the heading of Exophthalmic Goitre (p. 68), is continuing at Sheffield his well-known investigations of rickets which he began in London and at Cambridge and which last year formed the subject of a Report in the Council's series. The work is done in the new Field Laboratories of the University of Sheffield, erected last year by the University on a convenient country site near the city at a cost of about £7,000. The experimental work is brought into close and valuable relation to the clinical studies by Professor Mellanby and his colleagues in the medical and surgical wards of the Royal Infirmary, Sheffield. The Council would here cordially recognize the unusually complete facilities which the University of Sheffield has thus given to this scientific work and to its extension through clinical studies. The local Panel Committee have recently contributed £1,000 towards the cost of the Field Laboratories, and by this have given the most effective evidence of the interest taken by the medical practitioners of Sheffield in Professor Mellanby's work and of their sense of its value for the progress of medicine. The Council have continued to supply the chief expenses of this work, and their contribution has gained greatly in effectiveness through this generous local aid. More recently Professor Mellanby has been more particularly concerned with the relationship of the anti-rachitic food factor to calcium and phosphorus in the diet, with the relative rickets-producing effects of different cereals, and with the influence upon rickets of thyroid gland administered by the mouth. Further accounts of this work are being prepared for publication.

At the University of Leeds, Mr. Lowson and Mr. G. Winfield,

under the direction of Professor H. S. Raper, are determining the rate at which the chief inorganic salts in the body increase during growth. Figures for normal animals have been obtained and are being checked by further analyses, while changes produced by dietetic deficiencies are also under investigation. A part-time grant is being made to Mr. Lowson.

The results obtained by Dr. Corry Mann in his studies of rickets in South London, mentioned in previous Reports, have recently been published by the Council.

The work of Professor Korenchevsky in this subject at the Lister Institute, and of Miss Chick and her colleagues in Vienna, will be mentioned below under another head (pp. 60, 63).

Work by Dr. E. C. Dodds which also has a bearing on rickets is mentioned on p. 92.

At the Royal Hospital for Sick Children, Edinburgh, Mr. Norman M. Dott is continuing research work on the growth of cartilage with a view to the better guidance of surgery, which he began in collaboration with Mr. John Fraser. Special expenses are being met by the Council.

Leonard Findlay—
'A Review of the Work done by the Glasgow School on the Aetiology of Rickets.' *Lancet*, 29th April, 1922.
H. Corry Mann—
'Rickets; the Relative Importance of Environment and Diet as Factors of Causation: an Investigation in London.' *M. R. C. Special Report Series*, No. 68, 1922.
E. Mellanby—
'The Influence of Dietetic Factors on the Development of Rickets.' *Brit. M. J.*, 4th November, 1922.
D. Noël Paton—
'Rickets; A Theory of the Metabolic Disturbances and of its Association with Tetany.' *Ibid.*, 11th March, 1922.
'Rickets; the Part played by Unhygienic Conditions in Predisposing to the Disease.' *Glas. M. J.*, 1922, **97**, 129.
H. S. Hutchison—
'Rickets in India.' *Ibid.*, 1922, **97**, 145.
H. S. Hutchison, assisted by S. J. Shah—
'The Aetiology of Rickets, Early and Late.' *Quart. J. Med.*, 1922, **15**, 167.
J. S. Sharpe—
'The Phospholipin of the Blood and Liver in Experimental Rickets in Dogs.' *Bio-Chem. J.*, 1922, **16**, 486.
S. V. Telfer—
'Studies on Calcium and Phosphorus Metabolism.' *Quart. J. Med.*, 1922, **16**, 45.
'Studies on Calcium and Phosphorus Metabolism. Part II. The Metabolism of Calcium and Phosphorus in Rickets.' *Ibid.*, 1922, **16**, 63.
(See also pp. 62 and 65.)

Accessory Food Factors ('Vitamins').

The work on this subject has been continued under the direction of the Committee (p. 113) appointed jointly by the Council and the Lister Institute.

At the Lister Institute Dr. S. S. Zilva has continued his work in the whole-time service of the Council and under the general

direction of Professor A. Harden. Using various chemical and physico-chemical methods he has been engaged in the further study of the anti-scorbutic factor. With Professor Harden he has also been investigating the anti-scorbutic and anti-neuritic potency of malt in the various stages of the malting process, and the synthesis of the anti-scorbutic and anti-neuritic factors by lower organisms such as yeasts, algae, and moulds. With Dr. Bedson of the Lister Institute he has been studying the effects of 'Vitamin A' deficiency on the blood platelets. At the Great Ormond Street Hospital for Sick Children he has been engaged with Dr. G. F. Still in a clinical study of the therapeutic values of certain liver oils of which the vitamin potency had been experimentally determined. Dr. Zilva has also been associated with Dr. Drummond in the other investigations mentioned below.

A grant has again been made for the special expenses of work under the direction of Dr. J. C. Drummond at University College, London. Dr. Drummond and Dr. Zilva have together carried out further work on the nature of the substance or substances giving its valuable therapeutic qualities to cod-liver oil, and in this have used the numerous specimens of oil obtained during their visit to the Norwegian fishing-grounds last year. Their first problem was to trace the origin of the so-called vitamin A, which is held to be the active substance responsible for the beneficial effects obtained in the use of the oil. In collaboration with Dr. Lyster Jameson they have shown that simple marine diatoms growing in an artificial inorganic medium can produce relatively large amounts of the vitamin. This, together with a number of tests on other marine plants, some of which were made by Professor Hjort working in Professor Hopkins's laboratory at Cambridge, appears to show that the source of the vitamin A in marine organisms is the plant, and that there is therefore a relationship in the sea similar to that which has been traced between the terrestrial plants and animals. The diatoms do not, however, form the direct food supply of the species from which the liver oils are usually derived, and there are indeed several stages through which the vitamin appears to be transferred. The first of these is found in the minute animal organisms near the surface of the sea which feed directly on the microscopic plants, and which in turn constitute the food supply of numerous small kinds of fish or the young of larger kinds. The gadoid fishes, from which most of the medicinal liver oils are derived, feed chiefly on the smaller fish; in Norway at one season they feed almost entirely on the caplin, *Mallotus villosus*. That the fish store up the vitamin transferred in this manner from their food appears probable from some studies made by Dr. Drummond and Miss K. H. Coward, which have shown that young trout start life with a considerable reserve of vitamin A in the contents of their yolk-sac. This is apparently expended during the period when they are dependent on this food supply, and if, when they become dependent on external food,

this does not supply the vitamin, they cease to grow and ultimately die. But their development proceeds normally if foods rich in the vitamin are given.

Dr. Zilva and Dr. Drummond have also collaborated in a full investigation of the effect which the modern processes of manufacture of liver oils have on the vitamin value, of which the chief results have just been published. They have ascertained that there is very little loss of vitamin during the steaming processes which are now generally employed, and that the subsequent refining of the 'white oils' by freezing and filtering is equally free from harmful action. The popular conceptions that the brown oils represent the crude oils as they are prepared from the livers, and that the white oils represent the highly refined material, are erroneous. The brown oils are pigmented because they are prepared from more or less putrid livers, and these are seldom if ever refined to produce medicinal products, being usually sold for use in leather work or as cattle oils. The white oils are prepared from quite fresh livers. There are nevertheless wide variations in the vitamin values of different samples of cod or other fish liver oils, which may be due to the variations in the food supply of the fish, or to the seasonal variation in their physiological condition. In spite of these variations the poorest of these oils have been found to be many times richer in vitamin A than average samples of butter.

Dr. Zilva has visited Newfoundland during the past summer at the invitation of the Government of the Colony and has returned with much valuable material for investigation. During both these visits these representatives of the Council received every courtesy and the fullest facilities from the authorities and every assistance from the technical experts with whom they came in contact.

At University College Dr. Drummond and Miss Coward have made further studies of the chemistry of 'Vitamin A'. They have investigated the vitamin values of milk and butter in summer and in winter respectively. They had previously shown that the vitamin A value of butter is higher during grass feeding in summer than during winter feeding on roots, hay, and 'concentrates', and American workers have confirmed these observations as applicable to the milks yielded under corresponding conditions. As a natural sequel to this work they attempted during the last winter to investigate whether by giving a simple diet supplement to cows on winter feed the vitamin A value could be kept at summer level. The active co-operation of Captain J. Golding and Mr. J. Mackintosh of the National Research Institute in Dairying was obtained, and the experiment was made at Reading at the experimental farm attached to the Institute. The results have confirmed the previous observation that the vitamin A value of the butter falls rapidly when cows are brought indoors in winter and fed on a diet poor in that accessory factor. The effect of giving cod-liver oil as a supplement to a diet of hay, roots, and cake-

mixture was observed, and it is believed that good evidence of its value in raising the nutritive value of the butter has been obtained. The experiment is to be repeated during the coming winter. At Reading also, Dr. Drummond, Dr. Zilva, and Captain Golding have continued their studies of growth and rickets in pigs.

The whole-time grant to Professor V. Korenchevsky for work in the Department of Experimental Pathology at the Lister Institute has been maintained. Grants have also been made to Miss M. Soames, Miss M. Carr, and Miss Pickersgill, for work in the department under the direction of Dr. C. J. Martin, Director of the Institute. Professor Korenchevsky has completed his extensive observations upon experimental rickets in rats, a preliminary account of which was published last year. A full account of his results will appear in a report now in the press. From his extensive chemical and histological observations it is clear that vitamin A, or some other factor as yet not differentiated from it and of similar distribution in animal fats, exerts a controlling influence in the deposition of calcium in the skeleton. A deficiency of calcium and phosphates in the diet appears, from Dr. Korenchevsky's experimental results, which in this respect are confirmatory of those of McCollum and his co-workers in America, to play a contributory part. Professor Korenchevsky has also been studying the results of deficiency of vitamin A and calcium in the diet of the mother, during pregnancy and lactation, upon the subsequent development of the skeleton of the offspring, and he finds that it is possible, by modifying the diet of female rats in those directions, to control notably the production of rickets in the young animals after birth. A subsidiary investigation into the possible effects of saturated air and bad ventilation in causing rickets gave no indication that these environmental conditions exert any influence in the case of rats. Other work has been done upon the effects upon the content of vitamin A of aerating heated milk, with special reference to the effects of pasteurization upon the nutritive value of milk.

The quantitative relation of the anti-rachitic factor present in the diet to the deposition of calcium in the growing skeleton and the development of rachitic bones in rats is being studied at the Lister Institute by Dr. Goldblatt, Beit Memorial Fellow, with the assistance of Miss Soames provided by the Council. A report of the first series of experiments is being prepared for publication. Summarized briefly, the results show a close correspondence between the amount of vitamin A in the diet and the calcium content of the skeleton. Dr. Goldblatt is also endeavouring to ascertain the mode of action of light and ultra-violet rays in the prevention and cure of rickets.

Also at the Lister Institute, Dr. Ethel Luce, who received a part-time grant from the Council during a portion of last year, has completed a series of observations on the size and histology of the parathyroid gland in rats in relation to the age and weight

of the animals. The observations were undertaken as a preliminary to the study of the influence of dietary deficiencies upon this organ. Following on the recent discoveries of the influence of sunlight and ultra-violet radiations upon the phenomena of calcium deposition in animals and children, she is now engaged by prolonged experiment in finding whether the supply of vitamin A in cow's milk is entirely dependent upon that of the food which the animal consumes, or whether and to what extent the known seasonal variation in the milk in this respect is determined by the varying amount of sunlight acting on the cow at different times of the year.

An investigation of the values of different dietaries during the school age of life has been begun by Dr. H. Corry Mann, working in the whole-time service of the Council and with the assistance of Miss E. MacManus and Miss H. Vines. The field of work is a model village outside London where about six hundred boys of the industrial class are housed in separate homes each containing some thirty boys. The administrative council of this training school, while requesting that, at present, it should be named only as 'Station X', have given every facility for the undertaking, and quarters have been provided for a resident assistant. Three homes which were unoccupied when the work was begun have been assigned for the work, and these have been filled with three batches of boys—ninety boys in all—whose ages are between seven and twelve years and whose weights lie between 45 and 70 pounds. As far as possible an equal number of boys having similar age and weight have been drafted to each of the three houses, all of the boys being of English parentage. Repeated clinical examinations are made, and notes are taken of general development at regular intervals. During a preliminary period of four months the progress of all the boys was watched while they were consuming the basic diet of the village. Notes were taken both of the issue ration from stores and of the 'consumed ration' per boy. Food analyses of standard dishes and of various items of food have also been made, and sample rations from all meals have been weighed at table. An estimate has thus been obtained both of quality and caloric value of the individual rations eaten. After the preliminary period of four months, during which time all three houses received the basic diet, a change was made and two of the homes have since received additional items of food, the third home remaining on the basic diet as a control group of thirty boys. In one of the homes the additional item is fresh milk, which has been provided gratuitously by the United Dairies Combine. Observation is being maintained upon the consumed ration of all the boys in the three houses under the original or changed conditions of dietary, and it is proposed to continue the investigation for at least two years, the progress of the boys being noted. It may be added that this work was proposed to the Accessory Food Factors Committee by one of their members,

Dr. A. J. MacFadden of the Food Department of the Ministry of Health.

Dr. C. Da Fano, working at King's College, London, has done further work on the histo-pathology of the central nervous system and the ductless glands in vitamin deficiency, in addition to undertaking the other investigations mentioned below (p. 72). The work of Dr. J. C. Mottram and Dr. W. Cramer on the effects of radiation and of vitamin deficiency on the blood platelets is mentioned elsewhere (p. 88), as are also Dr. Wyon's researches into the influence of accessory food factors on bacterial growth (p. 91), and Mrs. Mellanby's studies of the part which diet plays in the development of teeth (p. 67).

K. H. Coward and J. C. Drummond—
'On the Significance of Vitamin A in the Nutrition of Fish.' *Bio-Chem. J.*, 1922, **16**, 631.

J. C. Drummond and R. K. Cannan—
'Tethelin—the Alleged Growth-controlling Substance of the Anterior Lobe of the Pituitary Gland.' *Ibid.*, 1922, **16**, 53.

J. C. Drummond, K. H. Coward, and A. F. Watson—
'Notes on the Factors influencing the Value of Milk and Butter as Sources of Vitamin A.' *Ibid.*, 1922, **15**, 540.

J. C. Drummond, G. P. Crowden, and E. L. G. Hill—
'Nutrition on High-Protein Dietaries.' *J. Physiol.*, 1922, **56**, 413.

J. C. Drummond and A. F. Watson—
'The testing of foodstuffs for Vitamins.' *Analyst*, 1922, 235.
'The sulphuric acid reaction for fish liver oils.' *Ib.*, 1922. (In the press.)

J. C. Drummond and S. S. Zilva—
'Studies of the Nutritive Value of the Edible Oils and Fats. 1. The oil-bearing seeds and crude vegetable oils and fats.' *Journ. Soc. Chem. Ind.*, 1922, **41**, 125.
'The modern processes of preparation of cod-liver oil and their effect on the vitamin value.' *Ibid.*, 1922.
'Fish-liver oils and other highly potent sources of Vitamin A.' *Lancet*, 24th June, 1922.

J. C. Drummond and S. S. Zilva, with the co-operation of K. H. Coward—
'The Origin of the Vitamin A in Fish Oils and Fish Liver Oils.' *Bio-Chem. J.*, 1922, **16**, 518.

H. L. Jameson, J. C. Drummond, and K. H. Coward—
'Synthesis of Vitamin A by a Marine Diatom (*Nitzschia closterium* W. Sm.) growing in Pure Culture.' *Ibid.*, 1922, **16**, 482.

V. Korenchevsky—
'Experimental Rickets in Rats.' *New York M. J.*, 1922, **115**, 612.
'The Influence of Parathyroidectomy on the Skeleton of Animals Normally Nourished, and on Rickets and Osteomalacia produced by Deficient Diet.' *J. Path. & Bacteriol.*, 1922, **25**, 366.
'The Aetiology and Pathology of Rickets from an experimental point of view.' *M. R. C. Special Report Series*, No. 71, 1922. (In the press.)

S. S. Zilva—
'Conditions of Inactivation of the Accessory Food Factors.' *Bio-Chem. J.*, 1922, **16**, 42.

S. S. Zilva and M. Miura—
'The Quantitative Estimation of the Fat-Soluble Factor.' *Ibid.*, 1922, **15**, 654.

S. S. Zilva, J. Golding, J. C. Drummond, and K. H. Coward—
'The Relation of the Fat-Soluble Factor to Rickets and Growth in Pigs.' *Ibid.*, 1922, **15**, 427.
'The Relation of the Fat-Soluble Factor to Rickets and Growth in Pigs. II.' *Ibid.*, 1922, **16**, 394.

S. S. Zilva and J. C. Drummond—
'Vitamin A content of Oils prepared from the livers of cod, coal fish, haddock.' *Lancet*, 8th October, 1921.

Studies in Deficiency Diseases in Central Europe.

The work on deficiency diseases, and more particularly on the aetiology of rickets, in Vienna has been continued during the past year with the joint support of the Medical Research Council and the Lister Institute. The work has consisted in the continuation and completion of the studies begun in the autumn of 1920. The staff has remained as before: Dr. Harriette Chick, a member of the staff of the Lister Institute, has again been in charge, and has been assisted by Miss E. M. Hume and Miss Henderson Smith, both receiving grants from the Council. The clinical members of the mission have been Dr. Elsie J. Dalyell, in the service of the Council, and Dr. Helen Mackay, Beit Memorial Fellow. The mission left Vienna on the completion of the work in last July after publishing a preliminary statement of the results obtained. The full report of the work in its different branches is now being prepared for publication.

The main energies of the staff during the period 1920–22 have been devoted to observations of the part played by diet in the prophylaxis of rickets in young infants. A description of the main scheme has already been given in preceding Annual Reports. The infants under observation were in-patients for periods varying from 6 to 18 months, partly at the University Kinderklinik, in a ward assigned to this work by the generous hospitality of Professor von Pirquet, and partly at the Amerikanische Kinderheilstätte, at Meidling, an institution also under the general direction of Professor von Pirquet. In the latter a hut was specially equipped for the purpose and was maintained from January 1921 to June 1922 by the Council with aid from a grant from the League of Red Cross Societies. The observations on prophylaxis have been made upon nearly 100 young infants, who were placed in two groups upon two contrasted diets, but under identical conditions of general management and hygiene. Diet I, the diet in general use for infants at the Kinderklinik, was high in calories, high in carbohydrate, low in fat, and low in vitamin A. Diet II was lower in total calories, lower in carbohydrate, richer in fat, and, as it also contained a daily ration of cod-liver oil, much richer in vitamin A. Both diets contained raw fruit or vegetable juices as an extra provision of vitamin C. The work was carried out in close collaboration with Dr. Hans Wimberger, Radiographer to the Kinderklinik, and in all children the development of the skeleton was observed by systematic X-ray photography.

The results of this observation on prophylaxis showed:—

(i) that slight but definite rickets was developed with great regularity, during winter upon Diet I, but not upon Diet II;

(ii) that it was not developed in summer upon either diet;

(iii) that the age of greatest susceptibility to the onset of rickets is during the first half-year of life.

Other studies here of the causation of rickets included those of curative measures used for infants, aged from 6 to 15 months, suffering from well-developed ' florid ' rickets on admission. In these cases the effects of treatment with (1) cod-liver oil ; (2) radiation from the mercury vapour quartz lamp ; and (3) sunshine out of doors, were studied, and comparison was made with the progress of similar infants maintained under identical conditions of diet as well as of general hygiene but not treated in any of these special ways. The results, as observed by systematic X-ray photography, showed that deposition of calcium occurred consistently in the epiphyses of children under any of these three forms of treatment, while negative results were obtained in the control children.

The results of these studies of prevention and cure, taken together, lead to the conclusion that quality of diet, especially absence of anti-rachitic element, is probably the most important factor in the causation of rickets in winter, and that sunshine may be the chief preventive factor in summer. They also show the importance of observing very young infants in all investigations upon the aetiology of rickets. These results confirm many important researches on the aetiology of rickets recently published in England and America in both the clinical and the experimental fields of inquiry. The proved importance for the cure and prophylaxis of rickets of sunshine on the one hand, and of cod-liver oil on the other, may serve to reconcile the hitherto apparently opposed points of view upheld by the adherents of the ' hygienic ' and ' dietetic ' theories, respectively. These researches also show the necessity for strict control not only of the qualitative details of diet, but also of meteorological condi ions, in all investigations in which nutrition may be even indirectly concerned.

Miss Hume has investigated at Vienna the relation of ultra-violet rays to vitamin A by means of experiments upon the growth of rats. This work is incomplete and is being continued at the Lister Institute. Important and interesting results have already been obtained, showing that while exposure to ultra-violet rays effects a striking economy in the use of vitamin A by the organism, it does not enable the animal to dispense altogether with this vitamin or to synthesize it for itself. Exposure to air through which the ultra-violet rays have passed i found to have effects similar to those obtained by exposure to the mercury vapour lamp's rays themselves. A preliminary account of these researches is now being prepared for publication. Other experimental work undertaken by Miss Hume includes studies of the relation of thyroid gland secretion to vitamin A in the growth and nutrition of rats (jointly with Dr. R. Wagner of the University Kinderklinik, Vienna), of the influence of the diet of the mother upon the vitamin content of her milk and the condition of her infant, and of the influence of diet and sunshine upon the vitamin content of cow's milk.

Other investigations in Vienna have included a large-scale observation by Dr. Dalyell and Dr. Mackay upon the value of cod-liver oil in the prevention of rickets among breast-fed and artificially-fed infants at the Landes-Zentralkinderheim, Vienna, with the permission of the director, Dr. Riether, and in collaboration with Dr. Max Zarfl, the physician in charge. With Dr. Wimberger of the Kinderklinik and Dr. Feller of the Pathological Institute, Dr. Dalyell and Dr. Mackay have also made post-mortem investigations in order to correlate the clinical signs of rickets with the conditions shown by radiographic and histological methods.

Harriette Chick and E. J. Dalyell—
'The Influence of Foods Rich in Accessory Factors in Stimulating Development in Backward Children.' *Brit. M. J.*, 24th December, 1921.
H. Chick, E. J. Dalyell, M. Hume and H. H. Smith—
'The Aetiology of Rickets in Infants.' (With a Note on the X-ray Diagnosis of Rickets by Hans Wimberger.) *Lancet*, 1st July, 1922.

Human Nutrition.

In consultation with the Ministry of Health a special committee (p. 117) has recently been appointed by the Council to advise upon the promotion of research work upon quantitative problems of human nutrition, as distinct from and supplementary to the qualitative problems dealt with by the Accessory Food Factors Committee (see above). This body will maintain supervision of the physiological directions of the work formerly assigned to a provisional committee which was appointed jointly by the Development Commission, the Medical Research Council, and the Department of Scientific and Industrial Research, and which in its turn took up certain questions arising from the work done during the war by the Food Committee of the Royal Society. The provisional joint committee has now been dissolved, other machinery already mentioned on p. 9 having been set up to secure co-ordination in fields of research in which more than one of the Departments just named are interested.

Under this heading may be mentioned also some investigations in progress in the Physiology Department of King's College for Women, London, where a grant is again being made for the expenses of work by Professor V. H. Mottram, Miss G. Hartwell, and Miss W. A. Clifford. Miss Hartwell has continued her work on the dietary factors that influence lactation and the growth of sucklings, and she has published papers showing that a diet containing a high proportion of any protein given to a nursing rat injures the health of the litter. She has shown that the effects vary within limits with the nature of the particular protein given. These high protein diets are unsuitable only during lactation. They appear, on the other hand, to be beneficial for growth, fertilization, or reproduction. The addition of milk in large quantities (100 c.c. per day per animal) to the diet protects

the offspring from this special danger from high protein diet during lactation. The search for the protective substance in milk showed, by elimination, that it is probably vitamin B—an unexpected result—much larger quantities of which are needed for dealing with amino-acids in the blood during lactation than in normal life.

Miss Clifford has published work on the estimation and distribution of carnosine in the animal kingdom among 100 different species examined. It is absent from the muscles of all invertebrates, those of some fishes, and of some birds. Otherwise it is present in all skeletal and cardiac muscles of the vertebrates. Her studies of this substance are directed to the interesting and practically important problems of the preservation of meat by various methods of cold storage, and they are supplementary to the work on that subject of the Food Investigation Board (Department of Scientific and Industrial Research).

W. M. Clifford—
'A Method for the Colorimetric Estimation of Carnosine.' *Bio-Chem. J.*, 1921, **15**, 400.
'The Distribution of Carnosine in the Animal Kingdom.' *Ibid.*, 1921, **15**, 725.
'The Effect of Cold Storage on the Carnosine Content of Muscle.' *Ibid.*, 1922, **16**, 341.
G. A. Hartwell—
'The Evil Effect of Excess Protein on Milk Secretion.' *Lancet*, 11th June, 1921.
'Excess Protein and Mammary Secretion.' *Bio-Chem. J.*, 1921, **15**, 563.
'Effect of Edestin on Mammary Secretion.' *Lancet*, 18th February, 1922.
'Antidote to the Toxic Effects of Excess Protein Diet during Lactation.' *Ibid.*, 4th November, 1922.
'Mammary Secretion, III. 1. The Quality and Quantity of Dietary Protein. 2. The Relation of Protein to other Dietary Constituents.' *Bio-Chem. J.*, 1922, **16**, 78.

Causes of Dental Disease.

The Committee on the Causes of Dental Disease which was appointed last year (p. 116) have held many meetings under the chairmanship of Professor W. D. Halliburton, and have initiated several investigations. Their first report is now in the press, and consists of three papers, on the development of enamel, by Mr. Howard Mummery, a member of the Committee. By permission of the Ministry of Health, Dr. J. M. Hamill continues to act as secretary.

Under the direction of a member of the Committee, Mr. Norman Bennett, data are being collected by a systematic examination of school children by Mr. N. J. Ainsworth, with a view to the settlement of particular problems. The Committee are indebted to the Board of Education and to numerous local authorities for facilities given for this work.

Mrs. Mellanby, also a member of the Committee, has continued

her experimental work at the Field Laboratories of the University of Sheffield (see p. 56 above) on the dietetic factors affecting the development of teeth, and the Council have maintained their part-time grant to her and have supplied the special expenses of the work. Mrs. Mellanby has recently extended her investigations to a study of dental defects in children, and work has been done with the effective co-operation of the School Medical Department of Sheffield. Endeavour has been made to ascertain whether there is any close correlation between the structure of deciduous teeth in children, as revealed by histological examination, and the tendency to decay. The results, which will shortly be published, are contrary to the views of many authorities and show that the deciduous teeth of these children are in general badly formed, and that, on the whole, badly formed teeth are more susceptible to caries.

J. Howard Mummery—
'The Structure of Teeth in Relation to Dental Disease' (Reports of the Committee for the Investigation of the Causes of Dental Disease, I). *M.R.C. Special Report Series*, No. 70, 1922. (In the press.)

Disorders of the Cardio-Vascular System.

Mention has already been made of the cardiological studies of Sir Thomas Lewis and his colleagues in the Council's Department of Experimental Medicine at University College, London (p. 33), and of some other work done in the medical unit at the London Hospital (p. 37).

Further expenses have been allowed for Professor J. B. Haycraft's work at the University of Cambridge on improvement of the methods for recording the pulse wave.

At the Royal Infirmary, Manchester, and in Professor A. V. Hill's department at the Victoria University, Dr. J. C. Bramwell has continued his clinical and experimental work on the time relations of the heart-beat and pulse. The Council have maintained their grant for part-time work and for special expenses.

The Council have again provided some expenses for the collection and publication of Professor J. A. MacWilliam's work, at the University of Aberdeen, on the physiology of the mammalian heart.

A part-time grant has recently been made to Dr. A. H. Holmes for work at the University of Manchester on the anatomy of the auricle of the bird's heart, with a view to the elucidation of some points which appear to be of fundamental physiological interest.

At the Victoria Infirmary, Glasgow, Dr. Ivy Mackenzie has done further work on syphilitic affections of the vascular system. This has included a study of eight cases of syphilis of the heart and aorta, and observations on the relation of syphilitic meningitis to acute cerebral *endarteritis obliterans* with symptoms of sudden onset. Pathological findings have been correlated with the previous clinical observations of the cases.

A part-time grant to Dr. Hubert J. Starling, of Norwich, has been continued. He has again been working upon disordered action of the heart, and the value of systolic murmur as a diagnostic sign in this condition. He has made a critical examination of the systolic murmurs in disordered action of infective and of emotional origin respectively, attempting to differentiate between murmurs due to functional and to organic causes, and to define their duration and the causation of their eventual disappearance. The work has involved a study of the effects of removing possible toxic foci, principally the tonsils, and this has led to further observations on the relation between infected tonsils, on the one hand, and organic heart disease, infective endocarditis, and rheumatic fever, on the other.

Dr. E. E. Laslett, who formerly held a grant from the Council for similar work at Hull, has reported to the Council on his further voluntary work on the influence of the vagus nerve upon the rhythm of the heart.

At the University of Bristol Dr. Carey F. Coombs has now concluded his work for the Council on the cardiac sequelae of rheumatic infection, and has published his results.

Carey F. Coombs—
'Streptococcal Infections of the Heart.' *Quart. J. Med.*, 1922, **15**, 114.

Exophthalmic Goitre (Graves's Disease).

The removal from Cambridge to Sheffield of Professor Edward Mellanby's experimental work on this and other subjects was completed early in the present year, and the Council have already referred on p. 56 to the good facilities provided for it at the new Field Laboratories of the University of Sheffield. As an extension of his previous work on the dietetic factors in the causation of rickets, Professor Mellanby has been making a closer study of the dietetic factors causing abnormal developments in the thyroid gland. As a member of the medical staff of the Royal Infirmary, he has been able to apply his results directly to the treatment of disease, more particularly of exophthalmic goitre, in patients, and results of great promise have already been obtained. The Council's grant for expenses and for the assistance of Miss D. Selby has been maintained.

At the Royal Free Hospital, London, Dr. G. S. Williamson has continued his work on the pathology of the thyroid gland, receiving a grant for expenses and the part-time assistance of Dr. I. H. Pearse provided by the Council.

As has already been mentioned, the Council are making a part-time grant to Dr. G. K. Stone for work on this subject with Mr. D. P. Dunhill in the Surgical Unit at St. Bartholomew's Hospital, London. The work has been undertaken with a view to testing the evidence brought forward by some workers that in

Graves's disease the thyroid yields a secretion differing qualitatively from the normal, as shown by the presence in the blood of antibodies to some constituent of the thyroid in these cases.

Disorders of the Respiratory System.

The Council have again met some special expenses of Sir J. Charlton Briscoe's work at King's College Hospital, London, on the mechanism of respiration.

Work on pulmonary tuberculosis is mentioned under the heading of that disease (p. 75), and the problems of dust inhalation are dealt with in Part VI under 'Industrial Diseases' (p. 104).

The Clinical Uses of Oxygen.

The Committee appointed to deal with anoxaemia and the clinical uses of oxygen have met less frequently this year, owing to the absence of Professor J. C. Meakins, who was taking part, with Mr. J. Barcroft, in the Royal Society expedition for the study of respiratory conditions at high altitudes in Peru. Pressure of other work has compelled Dr. D. K. Adams to relinquish his membership of the Committee, while Professor F. R. Fraser of St. Bartholomew's Hospital has been appointed an additional member.

At Guy's Hospital a large oxygen chamber has been used, in which a patient in bed can be kept, if necessary, under oxygen treatment for days, the expenses of the chamber being provided by the Council. Defects in the construction of the chamber have appeared in the course of work, and improvements have been effected. A long series of clinical observations are being made on the effects of oxygen treatment by this elaborate but complete mode of administration. During the past year Dr. J. M. H. Campbell, Dr. G. H. Hunt, and Dr. E. P. Poulton have also completed at Guy's Hospital part of the experimental work planned by the Committee on the causation of breathlessness. The clinical data already collected lead the Committee to the opinion that patients suffering primarily from damage to the lung receive benefit from treatment with oxygen, but that those with circulatory disorders receive little if any.

Professor J. C. Meakins, University of Edinburgh, has continued his tests of the utility of the more portable forms of apparatus devised for the administration of oxygen in disease. The Committee are convinced that, while the methods for administration of oxygen are being improved and its utility in certain conditions of disease is becoming more apparent (altogether apart from its universally recognized importance in general anaesthesia), the high cost of oxygen for medical purposes will nevertheless be a great obstacle to its extended employment. The cylinders into which it is usually compressed as a gas are heavy and awkward to use. The Committee believe that if the use of oxygen in hospitals and by the medical profession is to

become more general and efficient great improvements must be made in the apparatus of storage. It may prove to be best to depend upon liquid oxygen apparatus and to organize supply from special installations at different centres.

Dr. N. Morris, at the University of Glasgow, has studied during the year the various factors affecting the supply of oxygen to the body tissues. Experiments have been made to determine the influence of varying percentages of carbon dioxide in the inspired air upon the oxygen-saturation of the arterial blood in anoxaemia. He is at present engaged in work on the pulmonary blood-supply during anoxaemic conditions. The Council are making a grant for part-time work and for expenses.

J. C. Meakins—
' The Influence of Circulatory Disturbances on the Gaseous Exchange of the Blood. I. The Oxygen Saturation of the Arterial Blood in Tachycardia.' *Heart*, 1922, **9**, 185.
J. C. Meakins and H. W. Davies—
' The Influence of Circulatory Disturbances on the Gaseous Exchange in the Blood. II. A Method of Estimating the Circulation Rate in Man.' *Heart*, 1922, **9**, 191.
N. Morris—
' Anoxaemia and the Administration of Oxygen.' *J. Physiol.*, 1922, **56**, 283.
' Anoxaemia and the Increased Electrical Excitability of the Neuro-Myone.' *Brit. J. Exper. Path.*, 1922, **3**, 101.

Medical Problems of High Flying.

Major H. F. Pierce, who formerly received a whole-time grant from the Council for work at the University of Oxford under Professor Dreyer's direction, concluded during the past year the researches on the effects of reduced atmospheric pressure to which reference has been made in previous Reports.

Disorders of the Excretory System.

The work by Professor MacLean and his colleagues at St. Thomas's Hospital, London, has already been mentioned in Section III (p. 37).

A grant for the expenses of work on experimental nephritis has been made to Professor J. Shaw Dunn, formerly of the University of Birmingham and now of the University of Manchester.

A part-time grant, with expenses, has also been made to Dr. A. S. Strachan for work at the University of Glasgow on this subject.

During part of the year a personal grant was made to Dr. E. B. Verney for work on the factors determining urinary secretion, which he undertook in Professor Starling's laboratory at University College, London. Dr. Verney relinquished this part-time grant on his appointment as a Beit Memorial Fellow.

E. B. Verney and E. H. Starling—
' On Secretion by the Isolated Kidney.' *J. Physiol.*, 1922, **56**, 353.

Disorders of the Nervous System.

General Neurological Studies.

Further expenses have been provided by the Council for Professor T. Graham Brown's work at University College, Cardiff, on the physiology of the central nervous system. He has been studying problems in the function of the mid-brain, the orientation reactions of the eyes, and some properties of the spinal centre.

Dr. Ivy Mackenzie, in addition to the other work already mentioned (p. 67), has continued his studies of orthopaedic cases with anomalous motor and sensory disturbances of the limbs. The results will shortly be published.

For a few months during the past summer a personal grant was made to Dr. J. P. Hettwer of Harvard University, U.S.A., for the completion of an investigation under the direction of Sir Frederick Mott at the Maudsley Hospital, London, upon nervous co-ordination in voluntary movements. This work was done in collaboration with Dr. F. Golla.

The special Committee on Nerve Injuries (p. 114) have been collecting from war records and other sources data for a report on injuries of the spinal cord, thus continuing their work on injuries of the peripheral nerves which formed the subject of the report published by the Council last year. This second report will be ready for press at an early date, and injuries of the brain will thereafter engage the attention of the Committee.

T. Graham Brown—
'Gradual Manifestations of Affective Reactions.' *Encéphale*, 1921, **16**, 201.
'Inhibition and Excitation in Central Nervous System.' *J. Neurol. & Psychopath.*, 1922, **3**, 39.
F. Golla and J. Hettwer—
'The Influence of Various Conditions on the Time Relations of Tendon Reflexes in the Human Subject.' *Proc. Roy. Soc.*, 1922, B., **94**, 192.
G. Riddoch and E. F. Buzzard—
'Reflex Movements and Postural Reactions in Quadriplegia and Hemiplegia, with especial reference to those of the Upper Limb.' *Brain*, 1922, **44**, 397.

Disseminated Sclerosis.

The work of Dr. Gye and Mr. Dobell on this subject has already been mentioned in the section dealing with the National Institute (p. 23).

At the University and Western Infirmary, Glasgow, Dr. D. K. Adams has continued his work on disseminated sclerosis, a common and distressing form of progressive paralysis, with the co-operation of Dr. E. M. Dunlop, Dr. J. W. S. Blacklock, and Dr. W. H. Scott, and the Council have maintained the grants for part-time work and expenses made to these four investigators. During the past year the investigation into the aetiology of the disease has proceeded along clinical, therapeutic, and experimental

lines. Patients previously treated have been kept under observation, and further study has been made of the correlation of the symptoms of onset with the results of the colloidal gold test as a means of early recognition of the disease.

Neuro-syphilis.

The same investigators have made parallel observations on other nervous diseases, including neuro-syphilis : the conclusions drawn from an examination of 200 cases of this disease were incorporated in a paper read to the British Medical Association in July last. Efforts have also been made to determine, if possible, whether the changes in the cerebro-spinal fluid so frequently found in early stages of syphilis, even after prolonged treatment, form the starting-point of serious neuro-syphilis. The work has shown that complete modification of the conditions of both blood and cerebro-spinal fluid can be produced by intensive intravenous therapy even in cases of established central syphilis. The mechanism of the colloidal gold reaction has been further investigated, and a method for the standardization of colloidal gold has been devised and is yielding satisfactory results.

D. K. Adams—
' The Treatment of Neuro-Syphilis, with special reference to the Changes in the Cerebro-Spinal Fluid.' *Brit. M. J.*, 7th October, 1922.
D. K. Adams and W. H. Scott—
' The Colloidal Gold Reaction of the Cerebro-spinal Fluid ; Standardising and Application in Early Nervous Diseases.' *J. Path. & Bacteriol.*, 1922, **25**, 142.
E. M. Dunlop—
' The Wassermann Reaction in the Diagnosis and Control of Treatment of Nervous Syphilis.' *Brit. M. J.*, 7th October, 1922.

Lethargic Encephalitis.

At King's College, London, Dr. C. Da Fano has continued the investigations into the pathology of lethargic encephalitis for which the Council make a grant for part-time work and for expenses. This research was formerly part of an inquiry arranged jointly by the Ministry of Health and the Council, but the Ministry's field investigations have now been concluded and the results published. On the pathological and experimental sides, however, much still remains to be done.

In previous Reports some account has been given of Dr. Da Fano's investigations of the lesions found in cases of the disease and of the discovery in the brain tissues of certain intracellular structures provisionally called ' minute bodies '. During the past year much new material, both human and experimental, has been available for study. Specimens brought by Dr. Booth from Nigeria, where a lethargic disease not dissimilar from *encephalitis lethargica* is prevalent, have been carefully examined, and in a large number of them changes have been found almost identical in important respects with those found in lethargic encephalitis

occurring in this country. They showed other features, however, which were similar to those observed by v. Monakow and other authors in fatal cases of influenza complicated by an encephalitic process.

The experimental material has been obtained from Dr. J. R. Perdrau's work for the Ministry of Health at the Lambeth Infirmary, where he has found that the vesicular fluid from certain forms of skin affection (e. g. herpes) contains a virus capable of producing a disease in animals which is transmissible from one animal to another and produces fatal lesions, in many ways similar, as Dr. Da Fano has shown, to those of *encephalitis lethargica*. 'Minute bodies' have been found in the vesicular fluid of herpes and in the brain tissue of infected animals, and it is possible that the smallest of these structures may represent the virus itself. Further work is in progress, and the Council are now making a grant to Dr. Perdrau to aid his continued share in the investigation.

C Da Fano—
'Preparations from Cases of Epidemic (Lethargic) Encephalitis.' *Proc. Physiol. Soc., J. Physiol.*, 1921, **54**, cxiv.
'On Lethargic Encephalitis.' *Brit. M. J.*, 22nd October, 1921.
'Experimental Herpetic Encephalitis in Rabbits.' *Proc. Pathol. Soc., J. Path. & Bacteriol.*, 1922, **25**, 403.

Mental Disorders.

An account was given in the previous Report of the manner in which the Council co-operate with the Board of Control in promoting research work in mental disorders, and of the appointment of a special Committee (p. 116) on the subject under the chairmanship of Dr. Henry Head, a member of the Council.

At the University of Cambridge Miss L. G. Fildes has continued to receive a grant for whole-time research work on the causes of mental defect in children. The general aim which this investigation has in view is that of discovering whether, and if so, exactly what specific psychological characters exist which mark off a mentally defective from a mentally normal individual. A solution of this problem would help towards the better classification and the more advantageous treatment of mentally defective individuals, and it would throw valuable light upon normal mental functions. During the past year three main lines of investigation have been followed: (1) A study of word-association among defectives, involving work with nineteen defective individuals and an examination of some 9,400 verbal associations given by them; (2) a study of motor reaction, in which some 6,000 reactions given by thirty subjects have been analysed; (3) a more detailed study of certain individuals classified as mentally defective but showing certain peculiarities which would justify their inclusion in the special class of 'aphasics'.

Dr. D. Orr has done further work at the Lancashire County

Asylum, Prestwich, on the action of bacterial poisons on the nervous system, and the Council have maintained their part-time grant. The paper mentioned below has been published, and work is now being done on the function of the lipoid bodies secreted by the choroid plexus under the influence of toxic substances.

The former part-time grant to Dr. G. A. Watson, Lancashire County Asylum, Rainhill, has been renewed. Dr. Watson is investigating cases of microcephaly and the results of lesions of the corpus callosum of the brain.

The Council have maintained the grant for expenses formerly made to Sir Frederick Mott for work at the Maudsley Hospital, London. He is making a systematic investigation of the suprarenal glands with Dr. Emslie Hulton, and of the pituitary gland with Dr. Margaret Robertson. Sir Frederick Mott and Dr. Y. Barrada are studying the nervous and muscular systems in a case of *myasthenia gravis*, and Dr. F. Golla is continuing his objective study of neuroses and psychoses.

The chemical investigations formerly carried out at the Cardiff City Mental Hospital by Dr. R. V. Stanford have been expanded into a comprehensive scheme here for the study of the cerebrospinal fluid, in health and disease, from different aspects. This is under the direction of Dr. E. Goodall, Medical Superintendent, and the pathological work is in the charge of Dr. H. A. Scholberg. The Council are providing the salary of Mr. A. M. Wheatley, research assistant in the chemical laboratory.

Work in the same subject is also being done at the Lancashire County Asylum, Whittingham, by Dr. R. M. Stewart, to whom a grant for special apparatus has been made.

Grants formerly made by the General Board of Control for Scotland for the expenses of research work at the Scottish Western Asylums' Research Institute, Glasgow, and the Scottish Asylums' Pathological Laboratory, Larbert, have been provisionally continued by the Council by special arrangement.

Further expenses have been allowed to Dr. Ninian Bruce for a preliminary investigation of after-history records of functional nervous cases treated at War Hospitals in Scotland.

The Council are continuing the loan of certain apparatus to Dr. A. F. Hurst for work at Guy's Hospital, London, and to Dr. J. F. E. Prideaux for work at Addenbrooke's Hospital, Cambridge.

L. G. Fildes—
'A Psychological Enquiry into the Nature of the Condition known as Congenital Word-Blindness.' *Brain*, 1921, **44**, 286.
L. G. Fildes and C. S. Myers—
'Left-handedness and the Reversal of Letters.' *Brit. J. Psychol.*, 1922, **12**, 273.
F. W. Mott—
'Further Pathological Studies in Dementia Praecox, especially in relation to the Interstitial Cells of Leydig.' (Part I.) *Proc. Roy. Soc. Med.*, 1922, **15**, 1 (Sect. Psychiat.).

' The Reproductive Organs in Relation to Mental Disorders.' *Brit. M. J.*, 25th March, 1922.

F. W. Mott and T. Uno—

' Microscopic Examination of the Brain in Cases of "Surgical Shock".' *Proc. Roy. Soc. Med.*, 1922, **15**, 25 (Sect. Neurol.).

E. G. B. Calvert and S. A. Mann—

' Metabolism in Epilepsy compared with the Non-Epileptic as shown by Urinary Excretion.' *Arch. Neurol. & Psychiatry*, London, 1922, **8**.

S. A. Mann—

' Chemical Investigation of the Blood and Cerebrospinal Fluid in Epilepsy.' *Ibid.*, 1922, **8**.

M. Prados y Such—

' Further Pathological Studies in Dementia Praecox, especially in Relation to the Interstitial Cells of Leydig.' (Part II.) *Proc. Roy. Soc. Med.*, 1922, **15**, 1 (Sect. Psychiat.).

David Orr—

' Toxi-Infective Lesions in the Central Nervous System. The Influence of Disturbance of the Sympathetic Mechanism on their Localisation.' *Lancet*, 5th August, 1922.

Tuberculosis.

The study of Tuberculosis from many different aspects has been continued by a large number of different workers. The lines of study are co-ordinated by a Committee of the Council, under the chairmanship of Mr. C. J. Bond, and of this Dr. A. S. MacNalty continues to act as Secretary by permission of the Ministry of Health. The work in the different branches is in charge of sub-committees, of which the chief are the Bacteriological Sub-Committee, presided over by Major-General Sir William Leishman, a member of the Council, and the Tuberculin Sub-Committee under the chairmanship of Captain S. R. Douglas (p. 112). Further consideration of the occupational incidence of tuberculous disease has been assigned to the Industrial Health Statistics Committee (p. 105).

Bacteriological and Serological Studies.

At the University and Field Laboratories, Cambridge, Dr. A. Stanley Griffith has continued to give whole-time service to the Council, and his work has proceeded on the lines previously described. He has now completed the collection of another series of cases, 132 in number, of bone and joint tuberculosis. This new series has been examined not only for comparison with his former observations upon the incidence of bovine infections through milk in these forms of tuberculosis, but also in furtherance of his studies of the occurrence and distribution of strains of tubercle bacilli with aberrant characters. The proportion of cases due to tuberculosis of bovine type in this series is 13·6 per cent., that is, it is rather lower than in previous series. If the figures of this series are combined with those of previous series, it is found that the infection has been of bovine origin in rather more than 20 per cent. of the cases under 16 years of age and 6·5 per cent. of the cases over 16. Dr. Griffith has continued

throughout the year his work upon methods of producing immunity to the disease.

Dr. A. C. Inman has continued to receive a part-time grant for his work at the Brompton Hospital, London, on the morphology and agglutinability of the tubercle bacillus. Dr. R. G. Canti has now relinquished his grant for similar work at St. Bartholomew's Hospital, London, but continues to serve as a member of the Bacteriological Sub-Committee. With Dr. Lyon-Smith he is continuing his attempt to find a rapid means of identifying the tubercle bacillus in milk by staining methods which will differentiate it from other acid-fast bacilli.

In addition to his other work at the University of Glasgow, Dr. H. L. Coulthard has completed an investigation into the complement fixation reaction in tuberculous cases and will soon publish the results. In this he has compared the various forms of antigen which have been recommended, with a view to finding the most suitable ; and he has correlated the reaction quantitatively, so far as possible, with the diagnosis and the course of the disease in human tuberculosis and in experimental infections in animals.

Work on the bacteriology and serology of tuberculosis has recently been initiated by Professor W. J. Tulloch, University College, Dundee, and the Council are providing the whole-time assistance of Dr. G. R. Ross. Dr. W. T. Munro of the Fife and Kinross Sanatorium is giving his co-operation in this work.

Investigations undertaken for the Council by Dr. A. L. Punch, Dr. R. C. Wingfield, and Mr. W. H. Fearis, respectively, and mentioned in previous Reports, have been concluded during the period under review.

A. Stanley Griffith—
' The Cultural Characteristics and Virulence of Mammalian Tubercle Bacilli and the Circumstances under which they may vary.' *J. State Med.*, 1922, **30**, 139.
' Observations on the Biological Characters of *Leptospira Icterohaemorrhagiae*.' *J. State Med.*, 1922, **30**, 70.
H. L. Coulthard—
' The Complement Fixation Test in Tuberculosis.' (In the press.)

The Opsonic Index in Tuberculosis.

The Council have continued to make a grant to Miss C. M. Acland for assistance in the work of Colonel S. L. Cummins, David Davies Professor of Tuberculosis at University College, Cardiff. Colonel Cummins and Miss Acland have carried out, during the past year, a large series of observations upon the opsonic index, employing a modification of the method of Klein. They find, as previously noted by Sir Almroth Wright and other workers, that the phagocytosis induced by the undiluted or only slightly diluted serum of advanced and progressive cases is much less than that induced by the serum of normal persons or of ' well-balanced ' cases of the disease, and they have investigated the relations underlying this. They have found means of im-

proving the opsonic index test, and they now contemplate a fresh series of clinical observations with a view to showing whether the test, as modified, will give trustworthy results in diagnosis and prognosis.

The Pathology of Tuberculous Infection.

At the London Hospital, Dr. Charles Miller and Dr. H. M. Turnbull are continuing systematically their determination of the primary sites of infection in cases of children under ten years of age. A part-time grant for assistance in this work upon its bacteriological side, and for some independent studies, has been made to Dr. S. L. Baker, working at the Middlesex Hospital.

Grants have recently been made to Dr. S. Roodhouse Gloyne and Dr. D. S. Page for work on this subject at the City of London Hospital for Diseases of the Chest. The grant formerly held by Dr. G. Haswell Wilson at the University of Glasgow has been relinquished on his appointment as Professor of Pathology in the University of Birmingham.

Diagnosis and Treatment.

Dr. L. S. T. Burrell has continued to give part-time service to the Council at the Brompton Hospital, London. The Council have recently published a report which he has prepared with Dr. A. S. MacNalty on the value of artificial pneumothorax as a method of treatment in pulmonary tuberculosis, with a discussion of the attendant dangers and difficulties and of the groups of patients for which the method is suitable. An analysis of his first 150 cases is given, and the report includes a summary of the opinions of a number of other physicians who kindly replied to inquiries. In collaboration with Professor Dreyer, he has made further studies of the effects of pulmonary tuberculosis upon the 'Vital capacity' of the patient and the use of measurements of Vital capacity in diagnosis. He has also given assistance to Professor Dreyer in some new work on tuberculin.

Dr. Rowand's work at St. Andrews, on the early signs of tuberculous disease in children, has already been mentioned (p. 39).

L. S. T. Burrell and A. S. MacNalty—
'Artificial Pneumothorax.' *M.R.C. Special Report Series*, No. 67, 1922.

L. S. T. Burrell and Murray Y. Garden—
'Loss of Weight in Cases of Artificial Pneumothorax.' *Lancet*, 21st October, 1922.

Georges Dreyer and L. S. T. Burrell—
'The Vital Capacity Constants applied to the Study of Pulmonary Tuberculosis.' *Lancet*, 19th August, 1922.

Tuberculin.

During the early part of the year, the Tuberculin Sub-Committee (p. 112) were engaged in investigating various methods

of treatment of human tuberculosis by tuberculin and different preparations of tuberculin used in the treatment. The Sub-Committee are indebted to Dr. H. Hyslop Thomson, Dr. G. B. Dixon, and Dr. W. H. Wynn, who have communicated special reports on their experience of tuberculin treatment. The Sub-Committee have concluded, as the result of these and other studies, that until an accurate method for standardizing tuberculin is obtained, the administration of tuberculin can only be carried out empirically as a therapeutic measure, and the results in human tuberculosis cannot be evaluated or scientifically controlled. Professor G. Dreyer and Dr. H. K. Ward are accordingly continuing their researches in the Department of Pathology, University of Oxford, on the standardization of tuberculin. Professor S. L. Cummins, also, has been good enough to keep the Sub-Committee informed about the subcutaneous tuberculin tests which are being carried out for the Welsh National Memorial Associations, in which the object is to find whether the subcutaneous method of inoculation gives results of greater value for diagnosis than those of the von Pirquet skin reaction.

By far the greater part of the Committee's work has been given to an investigation into the efficacy of the various tuberculin tests in cattle. This has an important place in medical research in its relation both to the hygiene of the milk supply and to the catastrophes of bovine tuberculosis in children. The following new members have been added so that the Sub-Committee may have the benefit of their expert knowledge in this inquiry: Professor T. B. Wood, F.R.S., University of Cambridge; Mr. J. Mackintosh, of the National Institute for Research in Dairying, Reading; Mr. Wilfred Buckley, Secretary of the National Clean Milk Society, Dr. P. C. Varrier-Jones, and Mr. J. B. Buxton. Dr. A. W. J. MacFadden of the Ministry of Health, Colonel W. A. Wood, Mr. J. B. Tutt, and Mr. J. F. D. Tutt have given great help to the Committee by advice or by assistance in particular investigations. Lord Astor and Lord Elveden have been good enough to put information about the results of the tuberculin tests in their herds at the disposal of the Sub-Committee, and the National Farmers' Union has given cordial co-operation. Through the kindness of Mr. Wilfred Buckley an intensive investigation was undertaken by the Sub-Committee upon his herd at Moundsmeer Manor, Basingstoke. Sir Robert Robertson, of the Government Laboratory, kindly lent the services of Mr. J. R. Fraser, who made a chemical analysis of the constituents of the milk of the cows undergoing the test. Similar studies have been made of two herds in Hampshire and of the herd at the National Institute for Research in Dairying, Reading. In addition, the Sub-Committee have advised a number of cattle-owners upon the tuberculin test and have answered numerous individual inquiries upon the subject. Professor Dreyer is making special inquiries in France, Norway, and Denmark into detailed points in the experience of

workers using the test in these countries. The Sub-Committee hope to present a full report upon these various inquiries at an early date.

Chemotherapy in Tuberculosis.

At the University of Glasgow, Professor C. H. Browning has continued to work on this subject, and on cognate questions of the bactericidal powers of various antiseptics, with a grant for expenses and the whole-time services of Miss R. Gulbransen and Miss E. Meldrum provided by the Council. Professor J. B. Cohen, F.R.S., University of Leeds, has continued to receive a grant for his co-operation on the chemical side, and a grant has recently been made to Mr. G. H. Tatner for assistance in his work. Professor Browning and Miss Gulbransen have investigated some necessary preliminary problems in the normal behaviour of different strains of tubercle bacilli in experimental infections and of the effects of their continued passage through animals of the same species. Experimental tests of the curative value of various compounds, alone and with cod-liver oil, have been made. Professor Cohen has prepared a number of compounds of the cyanine dye group which have been found to have very powerful 'bacteriostatic' actions. Substances of this group have hitherto been used as photographic 'sensitizers', and their antiseptic properties do not appear to have been detected. The preparation and examination of further members of this group is in progress. The study of the action of the acridine compounds (acriflavine and proflavine) in localized pyogenic infections has been continued with special reference to their effect on processes of healing. With Dr. Charles Bennett, in charge of the patients, and Dr. J. W. S. Blacklock, the effects of these antiseptics have been observed in over 650 cases of burns of the third degree, cellulitis, osteomyelitis, and other conditions, as compared with those of other methods of treatment, and with special reference to the interference with formation of granulation tissue. There was no evidence in these cases of the pellicle formation or the necrosis described by some observers in war wounds. Histological examinations in a series of unselected cases confirmed and supplemented these clinical observations.

A grant has also been made for work in Professor Browning's laboratory to Dr. J. Ferguson Smith, who is ascertaining how far it is possible to introduce antiseptic substances into the depths of the tissues by the debated method of iontophoresis. He has found, both in animals and in the human subject, that no significant penetration occurs with such electric currents as can be borne, unless there is a gross breach of the epidermis. The method of antiseptic iontophoresis is also being used by Dr. Smith in the post-operative treatment of cases of tuberculous granulomata.

C. H. Browning—
'The Diagnosis and Treatment of Non-venereal Pyogenic Infections of the Urinary Tract, with Special Reference to Urinary Antiseptics.' *Glasgow M. J.*, 1922, **97**, 38.
'Experimental Work bearing on the Virulence of the Tubercle Bacillus and on the Localisation of Tuberculous Lesions in the Lungs.' (In the press.)
C. H. Browning and R. Gulbransen—
'An Interference Phenomenon in the Action of Chemotherapeutic Substances in Experimental Trypanosome Infections.' *J. Path. & Bacteriol.*, 1922, **25**, 395.
C. H. Browning, J. B. Cohen and R. Gulbransen—
'The Antiseptic Properties of Cyanine Dyes.' *Brit. M. J.*, 1st April, 1922.
C. H. Browning, J. B. Cohen, R. Gaunt and R. Gulbransen—
'Relationships between Antiseptic Action and Chemical Constitution with Special Reference to Compounds of the Pyridine, Quinoline, Acridine, and Phenazine Series.' *Proc. Roy. Soc.*, 1922, B., **93**, 329.
C. Bennett, J. W. S. Blacklock and C. H. Browning—
'The Action of Flavine Antiseptics on Localised Pyogenic Infections.' *Brit. M. J.*, 19th August, 1922.

General Treatment: Statistics and After-Histories.

Further records of the after-histories of sanatorium patients have been collected at the King Edward VII Sanatorium, Midhurst, the Brompton Hospital Sanatorium, Frimley, and the Peamount and Rossclare Sanatoria of the Women's National Health Association of Ireland. It is thought that by next year enough material will be available for a further report. The supplementary grant for the collection of family histories of patients at Midhurst has been continued for a second year, and the work on Sir St Clair Thomson's records of laryngeal tuberculosis is also still in progress.

Problems of heliotherapy are dealt with more particularly by the Committee on the Biological Actions of Light (p. 89), and questions on the occupational incidence of tuberculosis by the Committee on Industrial Health Statistics (p. 105).

The Electrical Sterilization of Milk.

Dr. F. C. Lewis has continued to receive a part-time grant for work on this subject with Professor J. M. Beattie at the University of Liverpool, in continuation of their earlier experiments of which the results were published by the Council. Dr. Lewis has also undertaken investigations into certain other bacteriological problems.

Influenza.

During the past year the Council have published the results of work by Professor James McIntosh, of the Middlesex Hospital, London, on the aetiology of influenza.

At the London Hospital Dr. P. Fildes has continued his investigations into the conditions of growth of *Bacillus influenzae* with a view to throwing more light upon the action of animal and

vegetable catalysts favouring growth. The Council have continued to make a personal grant and to provide the part-time assistance of Dr. Alice Greaves. Other work by Dr. Fildes is mentioned elsewhere (pp. 46, 83).

For some time past Dr. Gordon at St. Bartholomew's Hospital has been studying the bacteriology of influenzal pneumonia on behalf of the Council, so far as opportunities, which are necessarily intermittent in character, have occurred. An outbreak of influenza of a mild type in London during the early part of the current year (1922) provided material for studies mentioned earlier on p. 12, and Dr. Gordon reports that by making use of this opportunity he has succeeded in satisfying himself of the presence at this early stage of a minute filterable micro-organism similar to that described by previous observers. By cultures from the diluted and filtered secretion of the upper respiratory passages taken within 36 hours of the onset of fever, Dr. Gordon obtained evidence of the presence of this organism in 14 out of 20 cases examined by him, and in two out of three fatal cases he has cultivated it from the filtered bronchial secretion. In two recent cases Dr. Gordon believes that he has succeeded in demonstrating this minute micro-organism microscopically in the nasal secretion within 24 hours of the onset. The technical difficulties attending this work are great but the subject is being actively pursued. Dr. Gordon's other work is mentioned below.

M. H. Gordon—
'The Filter Passer of Influenza.' *J. Roy. Army Med. Corps*, 1922, **39**, 1.
'The Bacteriology of Influenza.' *Brit. M.J.*, 19th August, 1922.
J. McIntosh—
'Studies in the Aetiology of Epidemic Influenza.' *M.R.C., Special Report Series*, No. 63, 1922.

Studies of the Streptococcus and Pneumococcus Group.

The Council have again maintained the grant for part-time work and expenses made to Dr. M. H. Gordon at St. Bartholomew's Hospital, London. In addition to the studies of influenza just mentioned above, Dr. Gordon has further investigated the streptococcal infections. The study of the characters and clinical significance of pathogenic streptococci has been continued, chiefly by serological methods. Chief attention has been given during the past year to non-haemolytic strains. These streptococci normally abound in the saliva and in the alimentary canal: in disease they occur chiefly in the blood, and on the heart-valves in infective endocarditis. They have been suspected of playing an important part in some of the common forms of chronic or rheumatoid arthritis: and there is evidence that a micro-organism of this group is a factor in rheumatic fever. By their biological characters these non-haemolytic streptococci have long been divided into two main types, *S. salivarius* and

S. faecalis. The streptococci obtained by Dr. Gordon from cases of infective endocarditis have so far been found to belong mainly to the *S. salivarius* group, but a few cases have yielded *S. faecalis*. These endocarditis streptococci have been submitted to the agglutination and absorption test. It had been found in the previous year that while out of 114 specimens of haemolytic streptococci collected in various diseases no less than 107, when examined by this test, were found to conform to a single serological type. In contrast to this striking uniformity it is now found that 17 specimens of the non-haemolytic *S. salivarius* recovered from cases of endocarditis during the past year are separable by the same method into at least 14 distinct serological types ; and of 3 specimens of *S. faecalis* from similar cases, all were found to be distinct serologically from one another.

To gain further evidence than that given by agglutination tests, Dr. G. K. Stone, receiving a half-time grant, has been investigating with Dr. Gordon the problems of streptococcal infection by use of the complement fixation test. From present observations it would appear that while the complement fixation test is far more delicate than the agglutination test for identifying streptococcal infections, and has certain other advantages over it, it is less specific in the sense that infections by the three types *S. pyogenes*, *S. salivarius*, or *S. faecalis* are not differentiated so sharply or completely by complement fixation as by agglutination. The work is actively in progress, and Dr. Stone has succeeded in broadening the basis of the fixation test, and in increasing its range and thereby its clinical value for identifying cases of streptococcal infection. He has already succeeded in obtaining evidence of streptococcal infection in 11 out of 13 cases of chronic arthritis of unknown or doubtful aetiology investigated by use of the complement fixation test.

Dr. T. G. M. Hine, working in the whole-time service of the Council at St. Bartholomew's Hospital, has been assisting Dr. Gordon generally in his research work, and has continued his own studies of the staphylococci, using serological methods of differentiation.

Also working under Dr. Gordon's general direction at St. Bartholomew's Hospital, with a part-time grant from the Council, Dr. R. R. Armstrong has further advanced his study of serological types of pneumococci by use of the absorption of agglutinin test. The characters of the three chief types of pneumococcus and of some of their sub-types, to which the greater number of cases of pneumonia are due, have been defined. The relative prevalence of the various type infections in acute pneumococcal diseases has been determined by investigation of two hundred strains from various sources ; evidence is also adduced of a seasonal variation in the incidence of the several types. A paper describing these results is in course of publication. Dr. Armstrong is extending his work by a study of the protective effects

of sensitized vaccines with a view to their application in the treatment of pneumonia.

At the University of Liverpool Professor E. E. Glynn, has now completed, with Miss Lettice Digby, whose whole-time services were provided by the Council, an elaborate bacteriological and serological study of pneumococcal infections, already mentioned in previous Annual Reports. A full report upon this work will shortly be published.

Working at Addenbrooke's Hospital, Cambridge, in the whole-time service of the Council, Dr. J. F. Gaskell has continued his experimental and clinical studies of pneumococcal infections of the lungs. The experimental investigations have been especially directed to the modes in which the lungs offer resistance to infection, and of these the results, already published in part, will soon be presented more fully. The observations have been made by use of strains of Type I pneumococcus, and it appears therefore that the character of the lesion produced under different conditions of infection does not depend upon the type of the infecting organism but upon its virulence.

Dr. H. F. Moore, of University College, Dublin, concluded during the present year a study of the pathology of pneumonia for which the Council were making a part-time grant.

Rheumatic Fever.

Dr. Gordon's serological studies of streptococci (*vide supra*) are being supplemented on the clinical side by trials of streptococcal vaccines in cases of rheumatic fever. For this purpose part-time grants have again been made to Dr. G. Bourne and Dr. P. Hamill for work at the Queen's Hospital for Children and the Metropolitan Hospital, London, respectively. Previous work had seemed to show that these vaccines were not definitely effective during the course of an acute attack of rheumatic fever in children : the object of the present trials is to ascertain whether prophylactic inoculation during quiescent periods is useful for the arrest of disease and the avoidance of future acute attacks. The results already obtained are encouraging and the work is still in progress.

Diphtheria.

The Bacteriology Committee, of which the composition is given in the Appendix (p. 115), have made further progress during the year with what is at present their main task, namely, the preparation of a report upon diphtheria. Individual members of the Committee have undertaken various investigations needed for its completion. Among these may be named Captain S. R. Douglas, Secretary of the Committee, whose work at the National Institute has been mentioned (p. 19) ; Dr. P. Fildes, who has been working at this subject at the London Hospital in addition to his other investigations (pp. 46, 81) ; and Dr. C. G. L. Wolf,

who is working at the University of Cambridge on the influence of buffer salts upon the metabolism of *B. diphtheriae* as part of his more general studies of the conditions of bacterial growth (p. 91). A grant has also been made to Mrs. Barratt for work for the Committee at the Lister Institute, under the direction of Dr. J. C. G. Ledingham. Reference has already been made (p. 42) to work in the National Institute upon the standardization of diphtheria toxin. The report will be ready for publication at an early date.

Paul Fildes—
'The Nature of the Action of Potato upon the Growth of *B. influenzae*'. *Brit. J. Exper. Path.*, 1922, **3**, 210.

Venereal Diseases.

Gonorrhoea.

A grant has been made for the expenses of an investigation by Dr. David Lees, Edinburgh, into the value of the cuti-reaction in the diagnosis of gonorrhoea. The work is being done at the Royal Infirmary and the Pilton Hospital.

Professor W. J. Tulloch, University College, Dundee, has reported to the Council on the results, since published, of his studies of the gonococcus. The other work which he is now doing on the Council's behalf has been mentioned (p. 76).

A new edition of the Report No. 19, published by the Council in 1918, upon the laboratory diagnosis of gonococcal infections and the methods for the detection of the spirochaetes of syphilis is being prepared. Dr. G. T. Western, of the London Hospital, has undertaken the work of revision.

W. J. Tulloch—
'Serological Examination of One Hundred Strains of the Gonococcus.' *J. Path. & Bacteriol.*, 1922, **25**, 346.

Syphilis.

At the request of the Scottish Board of Health the Council have provided expenses for an inquiry by Dr. J. F. Dewar into the incidence of syphilis among the adult population in Scotland. A grant has also been made for the expenses of an inquiry into the incidence of congenital syphilis among children admitted to hospital: this work is being done in Glasgow under the direction of Dr. A. K. Chalmers and Dr. Leonard Findlay.

Under the direction of Professor E. E. Glynn, University of Liverpool, Dr. R. E. Roberts is now concluding his statistical and clinical investigation of the results of treatment of syphilis to which reference has been made in previous reports and for which a part-time grant has been made.

Dr. Ivy Mackenzie's work on cardiac lesions due to syphilis has already been mentioned (p. 67).

The investigations undertaken into the sero-diagnosis of

syphilis, with a special view to the standardization of methods, have been noticed under an earlier heading (p. 46).

The Committee (p. 113) upon the manufacture, biological testing, and clinical administration of salvarsan and its substitutes have now submitted their second report, published during the year by the Council. It deals with the occurrence of toxic effects following the administration of arsenobenzol preparations in the treatment of the disease. The Committee conclude that, while it is now well established that a considerably larger proportion of cures can be effected by salvarsan and its allied compounds than by any other form of treatment, there are, and will always be, exceptional individuals whose reactions to the drug will be more severe than is normal. The scrupulous physical examination of patients before treatment is urged as a means of still further reducing the small number of serious or fatal reactions. With that precaution, and with skilled administration of the drug, the chance of a fatal result probably does not exceed one in ten thousand. The very small number of unavoidable deaths due to this treatment are of course immeasurably outweighed by the reduction in deaths and disabilities which it has made possible.

The work of biologically testing samples of salvarsan preparations sold in this country has already been mentioned (p. 41).

Reports of the Salvarsan Committee—

II. 'Toxic Effects following the Employment of Arsenobenzol Preparations.' *M.R.C., Special Report Series*, No. 66, 1922.

Arthritis.

The personal grant to Dr. T. S. P. Strangeways, and the grant for the maintenance of his studies of rheumatoid arthritis and the methods of treatment at the Research Hospital, Cambridge, have been continued. He is attempting the better classification of the disease by the correlation of the clinical, naked eye, and microscopic changes found in its various types. With the assistance of Major Horne, I.M.S., an investigation is being made of the agglutinating properties of serum from patients suffering from rheumatoid arthritis, tested with different strains of streptococci. Vaccines have been prepared for patients from strains of streptococci which are agglutinated by the patient's serum. Other work by Dr. Strangeways is mentioned below (p. 94).

At the Royal College of Surgeons, St. Thomas's Hospital and elsewhere, Mr. A. G. T. Fisher, with a part-time grant from the Council, has continued his researches into problems of the anatomy and physiology of the joints, with special reference to the articular cartilage and inter-articular fibro-cartilages, their nutrition, and the healing of wounds in them. Some experimental work upon the physiology of the synovial membranes is also in progress. Studies are being made of the morbid anatomy and histology of osteoarthritis and some other allied chronic joint disorders.

These changes are being interpreted in the light of the anatomical and physiological investigations. It seems that the differences in behaviour of the central and lateral parts respectively of the articular cartilage in osteoarthritis can be largely accounted for by differences in their nutrition. An investigation of the earlier changes in the joints has revealed the fact that the condition is primarily inflammatory rather than degenerative. Evidence has been added to that already pointing to the important effects of toxic substances derived from chronic infective foci in the alimentary tract and elsewhere. Some of the results of this work have been published by Mr. Fisher in his Hunterian Lectures.

A. G. T. Fisher—

'Hunterian Lecture on Osteoarthritis: Pathology, Aetiology and Principles of Surgical Treatment.' *Lancet*, 1st and 8th July, 1922.

'A Contribution to the Pathology and Etiology of Osteo-Arthritis: with Observations upon the Principles underlying its Surgical Treatment.' *Brit. J. Surg.*, 1922, **10**, 52.

Malignant Disease.

The Council are continuing the part-time grant made to Dr. James Young for his work at the Royal Infirmary, Edinburgh, on the causation of cancer. By means of a coliform organism obtained from mouse and human carcinomata (and from cases of leukaemia) he has produced experimentally in about 75 per cent. of artificially infected mice a chronic and progressive lymphoid lesion of the nature of lymphoma and lymphosarcoma. The organism is obtained from cancerous growths by incubating the tissue in a highly acid medium, and, according to the investigator, it originates, in part at least, by the germination of round or oval bodies which are recognizable histologically in a section of cancerous growth. Dr. Young believes that by studying the lesions of the experimentally infected animals he has succeeded in tracing the evolution of the large oval or round bodies from the coliform phase. In his belief they correspond to the chlamydospores or conidia of the higher bacteria and fungi. He believes that, if the lesion he has produced is equivalent to a malignant growth, the experiments suggest that the only susceptible tissues in the healthy animal are those of the primitive mesodermic and lymphoid elements. The healthy epithelium may be insusceptible of infection and by subsequent experiment he is endeavouring to test his belief that only by a preceding irritation or damage can this insusceptibility be broken down. This view is in accord with the well-recognized clinical fact that cancer is often preceded by an irritation or damage of the corresponding epithelial surface.

At the Royal Cancer Hospital, Glasgow, Mr. A. N. Currie has been working at the significance of fat and lipochromes in the aetiology of cancer, and is beginning a study of the nitrogen and phosphorus exchanges of the cancer cell. A whole-time grant is being made.

A grant has been made for the expenses of tracing and recording the after-histories of patients treated for cancer of the colon and rectum at St. Mark's Hospital, London. The arrangements are in the hands of Mr. W. B. Gabriel.

Reference has already been made on p. 30 to a statistical investigation into the incidence of cancer in different trades and professions.

An account of the important studies on the use of radium which constitute the Council's largest contribution to the study of malignant disease, is given below in the section dealing with radiology.

A. N. Currie—
'The Fat of Adipose Tissue in Malignant Disease.' *J. Path. & Bacteriol.*, 1921, **25**, 213.

Radiology and Radiotherapy.

The Medical Uses of Radium.

The arrangements for the distribution to suitable centres of the radium bromide held by the Council for research purposes on behalf of the Government have been referred to in previous Annual Reports. The allocation has now been completed and a full year's work has already been done at those centres which first received fractions of the available quantity. Local research committees have been established at the different centres, and the Council have appointed a central Radiological Committee (p. 116) under the chairmanship of Sir Cuthbert Wallace. Of this Committee Professor Sidney Russ acts as Secretary, and to him and to Mr. F. Harrison Glew the Council have again been greatly indebted for much advice and practical help in the difficult technical problems incidental to the distribution of the radium.

An important fraction of the radium has been left at the Middlesex Hospital, where, as mentioned in previous Reports, the whole quantity was formerly used during the first phase of the scheme of research. The results of this phase of mass experimentation have now been published by the Council. Meanwhile new work with the remaining fraction has been carried out continuously. The clinical work is in the hands of the physicians and surgeons, under the chairmanship of Mr. T. H. Kellock, and the Council have continued their whole-time grant to Dr. Helen Chambers for assistance in this and for her correlated experimental studies. The pathological and physical work remains in the hands of Professor W. S. Lazarus-Barlow and Professor Sidney Russ, respectively. The Council continue to provide an assistant, Miss D. Clephan.

At University College Hospital, London, the treatment is being employed chiefly for malignant disease of the uterus and

in cases of menorrhagia. The work is being done by a committee of the hospital staff under the chairmanship of Dr. G. Blacker, and the manipulation of the radium has been in the hands of Mr. J. B. Hunter, Harker Smith Registrar.

Three subjects of investigation have been followed at St. Bartholomew's Hospital, London, namely treatment of sarcomata by Professor G. E. Gask and Mr. G. F. Keynes, treatment of carcinomata of the cervix uteri by Mr. Malcolm Donaldson and Dr. R. G. Canti, and treatment of malignant growths of the naso-pharynx, larynx, and oesophagus, by Mr. Douglas Harmer and Mr. T. H. Just.

Carcinomata of the uterus and breast, rodent ulcers, and naevi have been the principal types treated at King's College Hospital, London, where Dr. Robert Knox is the radiologist in charge. The radium here has also been made available for experimental work on the effects of radiation on the body tissues, for which the Council are making a part-time grant to Dr. H. A. Colwell.

A fraction of radium has recently been allotted to the London Hospital. It is being used in diseases of the skin by Dr. J. H. Sequeira, and in malignant diseases of the uterus by Mr. S. G. Luker.

Work at the King Edward VII Hospital, Cardiff, at the General Hospital, Birmingham, and at the Royal Infirmary, Aberdeen, has been recently begun. The radium salt assigned for work in Aberdeen is also being used for experiments by Dr. J. Cruickshank in the University. For assistance in this and other work a part-time grant has been made to Dr. D. W. Berry.

One of the earliest allocations of radium was that made to the Irish Public Health Council on the application of Sir E. Coey Bigger. The work here differs from the investigations already mentioned, in that it is done with radium emanation issued from a central laboratory in Dublin, where the radium is kept for the purpose under the direction of Professor J. Joly, F.R.S. The emanation is issued to certain hospitals and private practitioners throughout the country, and records are made of the results obtained.

A fraction has also been allotted for experimental purposes to the Radium Institute, London, where Dr. J. C. Mottram is studying the effects of radiation upon the testes, the pituitary gland, the thyroid glands, and the blood-platelets, and upon fat absorption in the intestine. Dr. William Cramer and Dr. A. H. Drew of the Imperial Cancer Research Fund have been associated with Dr. Mottram in part of this work, and the Council have made a grant to Dr. A. N. Kingsbury of the Middlesex Hospital for co-operation in some bacteriological problems that have incidentally arisen. It was mentioned in the last Annual Report that a fraction of this radium salt had been allotted to Sir Ernest Rutherford, F.R.S., for experimental work at the Cavendish Laboratory, University of Cambridge.

Sidney Russ, W. S. Lazarus-Barlow and others—
'Medical Uses of Radium: Studies of the Effects of Gamma Rays from a Large Quantity of Radium.' *M.R.C., Special Report Series*, No. 62, 1922.
J. C. Mottram, W. Cramer and A. H. Drew—
'Vitamins, Exposure to Radium and Intestinal Fat Absorption.' *Brit. J. Exper. Path.*, 1922, **3**, 179.
H. H. Poole—
'On the Distribution of Activity in Radium Therapy under Different Conditions of Screening.' *Scient. Proc. Roy. Dub. Soc.*, 1922, **26**, (N.S.), 467.

Radiography.

A grant has been made for the expenses of a radiographic study of the movements of the pylorus and duodenum which Sir Archibald D. Reid is making at St. Thomas's Hospital, London, in association with Professor Hugh MacLean and Sir Cuthbert Wallace.

THE BIOLOGICAL ACTIONS OF LIGHT.

The Council have long had in view the more active promotion and better co-ordination of the scattered inquiries into the actions of light upon the human body in health and disease which have recently been undertaken in various directions. Prominent among these have been studies of sunlight treatment in tuberculosis and other diseases, and at many points work of this kind has been impeded by want of accurate knowledge of the actions of light, whether beneficial or harmful, upon the various animal tissues and organs, upon the chemical substances composing them, and upon invading bacteria or other parasites. In January last the Council appointed a Committee (p. 116) under the Chairmanship of Professor Sir William Bayliss, F.R.S., to advise them generally upon investigations into the biological actions of light. The word 'light' is not restricted here to the rays of the visible spectrum, and arrangements have been made to bring the work of this Committee into effective touch with that of the Radiology Committee already mentioned.

This Committee have already made plans for immediate investigations of the specific effects of light and of its different constituent rays on the body fluids and tissues and their simpler components, and on bacteria and protozoa both within the body and outside it. Some parts of this work have been in progress at the National Institute throughout the year. Mr. Barnard, in his Optical Department, is giving great assistance to the work of the Committee by the design and preparation of suitable apparatus and by his work in spectrophotometry and other methods. Captain Douglas is conducting preliminary experiments upon the effects of light rays in raising or lowering the resistance of animal tissues to bacterial invasion. Sir Henry Gauvain's studies of sunlight treatment, in association with which Dr. Leonard Hill and his colleagues have done much interesting collateral work, have been mentioned in previous Reports. Dr. Hill has been continuing his studies of the conditions under which erythema and pigmentation are produced in the skin on exposure to the sun's rays and the

effects in raising the temperature of the skin and the underlying organs by exposure to the sun or to the carbon-arc lamp. Mr. Webster, in his department, is determining the action of ultra-violet light on the blood *in vitro*, and is investigating the changes in protein exposed to light.

A grant has been made by the Council to Dr. D. T. Harris, working in Sir William Bayliss's laboratory at University College, London, for the special expenses of an investigation of certain photo-chemical reactions in the tissues.

A part-time grant has been made to Dr. R. G. Bannermann, who is undertaking observations at Montana, Switzerland, on the effects of light on the blood platelets.

Some of the most interesting and significant work done during the year has sprung from the studies made in Vienna by Miss Chick and her colleagues upon the effects of sunlight and of artificial light in the prevention or cure of rickets and the comparison of these actions of light with the effects of vitamin deficiency in the diet. These have been mentioned already on p. 64. A closer analysis of the meaning of these clinical observations has been undertaken by Miss Margaret Hume, in the whole-time service of the Council, both at Vienna and more recently in Professor C. J. Martin's department at the Lister Institute, where she is making an experimental inquiry into the effects of light of various kinds upon rats under various conditions of diet. Other work in the same field is also in progress under Professor Martin's direction. Work upon similar lines to that of Miss Hume is being done by Dr. Leonard Hill and his colleagues at the National Institute. There is good ground for hope that results of the greatest practical importance and biological interest will be the early outcome of these investigations.

General Biochemical Researches.

Bacterial Chemistry.

At the University of Cambridge whole-time grants are being made to Mrs. Callow (formerly Miss Barbara Clark) and Miss M. Stephenson for work under Professor Gowland Hopkins. Mrs. Callow is engaged upon studies of bacterial life in the absence of oxygen, and in particular upon a comparative study of the enzymes of aerobic and anaerobic organisms, which has led to interesting results shortly to be published. Miss Stephenson is continuing the work on the chemical exchanges of bacteria which she began when a Beit Memorial Fellow, determining by exact methods the quantitative changes in the culture medium of a given bacillus and its production of fats, lipoids, carbohydrate and protein. She is investigating the ability of the organism to use various types of organic compounds under different conditions, and the relation of this to the phenomena of fat formation and the connected physical characters of the bacillus.

Also at the University of Cambridge Dr. C. G. L. Wolf, in the whole-time service of the Council, has been tracing the influence of ' buffer salts ' on the metabolism of the diphtheria bacillus, the influence of various factors on the growth of the meningococcus, and the effects of the surface tension of the culture medium on the growth of bacteria. His work on the diphtheria bacillus forms part of the scheme of work (p. 83) undertaken by the Bacteriological Committee. He has published the papers mentioned below.

Expenses have been granted for work at the University of Bristol by Professor I. Walker Hall and Dr. A. D. Fraser. With the assistance of Professor J. W. McBain and Miss M. Kieser, Professor Walker Hall has made a study of indicators for use in estimating the reaction of bacterial cultural media, and with Dr. Fraser he has been working at the results obtainable with blood cultures. The papers mentioned below have been published.

Dr. G. A. Wyon, upon his appointment as a University Lecturer, has now relinquished his grant from the Council for work with Professor J. W. McLeod at the University of Leeds on the influence of accessory food factors on bacterial growth.

Dr. W. H. Tytler has completed his work at the National Institute for Medical Research, to which reference has already been made (p. 22), upon receiving an appointment in the Welsh National School of Medicine at Cardiff.

Mention has also been made (p. 22) of Dr. Laidlaw's work at the National Institute.

I. Walker Hall—
' Indicators for Culture Media Containing Varying Acids and Buffers.' *Brit. J. Exper. Path.*, 1922, **3**, 182.
' Action of Dilute Acids in Blood Cultures.' *J. Path. & Bacteriol.*, 1922, **25**, 297.
I. Walker Hall and A. D. Fraser—
' The Action of Dilute Acids upon Bacterial Growth in Optimum Hydrogen-ion Concentration.' *Ibid.*, 1922, **25**, 19.
C. G. L. Wolf—
' The Mechanism of the Reversal in Reaction of a Medium which takes place during growth of *B. diphtheriae*.' *Bio-Chem. J.*, 1922, **16**, 541.
' The Influence of the Quality of the Meat used upon the Reaction Curve of a Nutrient Medium.' *Brit. J. Exper. Path.*, 1922, **3**, 295.
C. G. L. Wolf and E. K. Rideal—
' The Properties of Dibenzoylcystine.' *Bio-Chem. J.*, 1922, **16**, 548.

Oxidation in the Tissues.

The Council continue to provide the special expenses of work by Professor Gowland Hopkins, F.R.S., at the University of Cambridge. He is continuing his studies of the chemical mechanism controlling oxidations in the tissues. It has been shown that the dipeptide glutathione constitutes, with certain structural elements in the tissues, a non-enzymic and oxidation-reduction system of special type, not acting as a ferment and stable under wide temperature ranges. It is being shown that some instances

of oxidation in the tissues previously thought to be due to ferments (oxidases) really depend upon another type of chemical agent (catalysts) acting with the elements of water. Other cases are being studied and it is believed that some important generalizations will be established.

Responses to Meals.

The part-time grant to Dr. E. C. Dodds, for work at the Middlesex Hospital, London, has been maintained. With Mr. T. Izod Bennett he has continued his studies of the variations in alveolar carbonic dioxide tension following meals, both in normal and in various pathological conditions. With Professor J. McIntosh he has investigated the blood changes, and with Dr. E. L. Kennaway the urinary diastase reaction, during tests of the efficiency of the liver, and has continued the investigations, mentioned last year, into the possible existence of pancreatic disorder in rickets. The following papers have been published :—

E. C. Dodds—
' Evidence of Pancreatic Disorder in Rickets.' *Brit. M. J.*, 1st April, 1922.
' Variations in the Diastatic Power of the Urine in Relation to its Reaction, with a Suggested Method for the Estimation of the Diastase Content.' *Brit. J. Exper. Path.*, 1922, **3**, 133.

E. C. Dodds and T. Izod Bennett—
' Variations in Alveolar Carbon Dioxide Pressure in Relation to Meals : A Further Study.' *J. Physiol.*, 1921, **55**, 381.

T. I. Bennett and E. C. Dodds—
' A Contribution to the Study of the Mechanism of Secretion in the Upper Alimentary Tract.' *Intern. J. Gastro-Enterology*, August, 1921.
' On Certain Conditions Associated with Deficient Secretion in the Upper Alimentary Tract.' *Lancet*, 10th June, 1922.
' Observations on Secretion into the Stomach and Duodenum : With Special Reference to Diabetes Mellitus.' *Brit. M. J.*, 7th January, 1922.

Diabetes.

At King's College Hospital, London, Dr. G. A. Harrison has continued the combined clinical and laboratory work on *diabetes mellitus*, for which the Council make a part-time grant, and has paid special attention to the results of treatment by carefully balanced diets. As judged by renal function tests the kidneys of most diabetics are found to be ' efficient '. Confirmation has repeatedly been obtained of the great clinical value of blood-sugar curves in revealing the nature of mild degrees of glycosuria. Of these studies some have been made with Dr. R. D. Lawrence ; the results will shortly be published.

Towards the close of the year under review the Council sent representatives to Canada to study the new insulin treatment developed at the University of Toronto. Reference has already been made (p. 14) to this important work, of which the further development and practical applications in this country will be the objects of studies now in course of arrangement in the National Institute and at other centres of work.

G. A. Harrison—
'Urea Tests of Renal Function.' *Brit. J. Exper. Path.*, 1922, **3**, 28.
'Glycosuria in Renal Disorders.' *Proc. Roy. Soc. Med.* (Sect. Urol.), 1922, **15**, 39.
'Observations on Postural Proteinuria.' *Lancet*, 12th November 1921.
G. A. Harrison and R. D. Lawrence—
'Diastase in Blood and Urine as a Measure of Renal Efficiency.' (In the press.)

Efficiency of Hepatic Function.

Dr. R. L. Mackenzie Wallis has received a part-time grant for work at St. Bartholomew's Hospital, London, upon tests used in the diagnosis of liver insufficiency. This was undertaken originally for the investigation of the effects of arsenobenzol (Salvarsan) compounds upon the liver, and the conclusions upon that subject have been published in the Second Report of the Salvarsan Committee (p. 85). It has seemed useful to extend the inquiry, and the effects of various diseases of the liver are being followed by the laevulose tolerance test and by reference to the lipase and cholesterol content of the blood serum.

Distribution of Glycogen and other Carbohydrates in the body

A grant has recently been made for work on this and some connected subjects by Mr. W. K. Slater, under the direction of Professor A. V. Hill, F.R.S., in the University of Manchester.

The Council have made a grant for the special expenses of a study of the carbohydrate content of brain substance which is being undertaken by Mr. J. Pryde at University College, Cardiff.

Properties of Haemoglobin.

The Committee (p. 114), appointed to deal with this subject have completed a report on the acid-base equilibrium of the blood which is now in the press.

Grants for work on the subject, generally supervised by the Committee, are being made to Mr. J. Barcroft, F.R.S., and to Mr. T. R. Parsons, University of Cambridge ; to Dr. E. P. Poulton and assistants, Guy's Hospital, London ; to Mr. W. E. L. Brown and Miss R. E. Conway, under the direction of Professor A. V. Hill, University of Manchester ; and to Miss E. M. Hickman, under the direction of Dr. W. MacAdam, University of Leeds.

Haemoglobin Committee
'The Acid-Base Equilibrium of the Blood.' *M.R.C. Special Report Series*, No. 72 (In the press.)
J. Barcroft, A. V. Bock, A. V. Hill, T. R. Parsons, W. Parsons, and R. Shoji—
'On the Hydrogen-ion Concentration and some Related Properties of Normal Human Blood.' *J. Physiol.*, 1922, **56**, 157.
Ruth E. Conway and Florence V. Stephen—
'The Reaction of Blood.' *J. Physiol., Proc. Physiol. Soc.*, 1922, **56**, xxv.
T. R. Parsons and Winifred Parsons—
'The Relations of Carbon Dioxide in Acidified Blood.' *J. Physiol.*, 1922, **56**, 1.

Diuretics.

A grant has been made to Dr. Mona Kirkhouse for work, under the direction of Dr. W. E. Hume at the Victoria Hospital, Newcastle-on-Tyne, on the physiological effects and clinical value of various drugs of this class.

Cinchona Derivatives and Malaria.

In previous Reports reference has been made to the work of a Committee (p. 114) appointed to investigate the curative value in malaria of the various cinchona alkaloids allied to quinine. Facilities have been granted by the Colonial Office and by the Sudan Government for an extension of this work at some centres in the tropics, which is now being arranged.

The Use of Pituitary Extract in Child-birth.

The Council have provided further expenses for the work of the Committee (p. 116) appointed jointly with the Royal Society of Medicine (Section of Obstetrics and Gynaecology) to deal with this question.

Work upon the standardization of pituitary extracts has been mentioned already (p. 18).

General Physiological and Pathological Researches.

Artificial Culture of Surviving Animal Tissues.

The Council have made a part-time grant to Mr. H. M. Carleton for assistance in work by Sir Charles Sherrington, President of the Royal Society, at the University of Oxford, on the growth of isolated animal tissues *in vitro*.

Dr. Strangeways has investigated, in the course of his work on rheumatoid arthritis (p. 85) at Cambridge, some very striking phenomena shown by surviving tissues and tissue-cells, and has communicated some of his observations to the Royal Society.

Sizes of Red Blood Cells.

At University College Hospital, London, Dr. C. Price-Jones has continued to receive a grant for studies of the variations in size shown by the red cells in various conditions. In particular he has observed the deviations from the normal found in pernicious anaemia and in anaemia following haemorrhage, and is making similar studies in cases of emphysema cardiac disease, and polycythaemia rubra. With Professor A. E. Boycott he has studied, experimentally, the influence of anaesthesia on the restoration of blood-volume after haemorrhage and after transfusion.

C. Price-Jones—
'The Diameters of Red Cells in Pernicious Anaemia and in Anaemia following Haemorrhage.' *J. Path. & Bacteriol.*, 1922, **25**, 487.
A. E. Boycott and C. Price-Jones—
'The Influence of Anaesthesia on the Restoration of the Volume of the Blood after Haemorrhage and after Transfusion.' *Ibid.*, 1922, **25**, 335.

Histology of Nerve Endings in Muscle.

A part-time grant for work on this subject has recently been made to a distinguished Russian histologist, Dr. Nicolas Kulchitsky, formerly a professor in the University of Petrograd and Minister of Education to the late Czar. The work is being done in Professor Elliot-Smith's department at University College, London.

Physiology of Digestion and Absorption.

In Professor Starling's laboratory at University College, London, Dr. G. V. Anrep continues to receive a grant for part-time work and expenses. In particular he has been studying the nitrogen and sugar exchanges of the salivary glands, at rest and during secretion, and the associated nervous mechanisms. Several papers have been published, and others will shortly be in the press.

G. V. Anrep—
'Observations on Augmented Salivary Secretion.' *J. Physiol.*, 1922, **56**, 263.
G. V. Anrep and R. K. Cannan—
'The Metabolism of the Salivary Glands. II. The Blood Sugar Metabolism of the Submaxillary Gland.' *Ibid.*, 1922, **56**, 248.

The Properties of Serum.

Expenses have again been provided for Dr. J. Holker's work at the University of Manchester on the physico-chemical properties of blood serum in health and in disease. An investigation of the interaction of serum with the antigen used in the Wassermann test has led to a new and interesting observation that a remarkable periodic change in the aggregation of a colloid in the presence of progressively increasing concentrations of an electrolyte is shown by all colloids, whether of the emulsoid or suspensoid type and whether of organic or inorganic origin. This may have an important bearing on the mechanism of immunity and other reactions in which colloid substances play a part.

J. Holker—
'The Properties of Syphilitic Sera in Relation to the Specificity of Immunity Reactions.' *J. Path. & Bacteriol.*, 1922, **25**, 281.
'The Opacity of a Mixture of Serum and Wassermann "Antigen" in Progressively Increasing Concentration of Sodium Chloride.' *Ibid.*, 1922, **25**, 291.
'The Periodic Opacity of Wassermann "Antigen" in Progressively Increasing Concentrations of Sodium Chloride.' *Ibid.*, 1922, **25**, 522.

Blood and Liver Changes in Anaphylactic Shock.

A whole-time grant has recently been made to Dr. R. A. Webb for his assistance in work on this subject by Professor H. R. Dean, University of Cambridge.

H. R. Dean—
' The Histology of a Case of Anaphylactic Shock Occurring in a Man.' *J. Path. & Bacteriol.*, 1922, **25**, 305.

Changes in Bacteria under varying conditions of Environment.

With a part-time grant from the Council, Professor E. W. Ainley Walker, University of Oxford, has continued his studies in this subject.

The results of work with Dr. A. D. Gardner (p. 45) on the serological changes produced in bacteria of the enteric and dysenteric groups by repeated sub-culture in the presence of specific agglutinating sera have now been published. A mucoid form of *B. paratyphosus* B experimentally produced last year has been further investigated. Other experiments have been undertaken to find the extent to which bacteria, growing in media free from fat and sugar, are capable of producing fat from protein, and to define in new directions the conditions for maintaining vitality and growth in the cultivation of the more delicate and more highly parasitic organisms.

E. W. Ainley Walker and A. D. Gardner—
' An Inquiry into the Nature of the Serological Differences Exhibited by Different Cultures of a Bacterial Species (*B. typhosus*).' *J. Hyg.*, 1921, **20**, 110.
E. W. Ainley Walker—
' Studies in Bacterial Variability. On the Occurrence and Development of Dys-agglutinable, Eu-agglutinable, and Hyper-agglutinable Forms of Certain Bacteria.' *Proc. Roy. Soc.*, 1922, B., **93**, 54.
' Studies in Bacterial Variability. The Experimental Production of a Mucoid Form of *B. paratyphosus* B.' *J. Hyg.*, 1922, **21**, 87.
' The Formation of Fat from Protein.' *Proc. Physiol. Soc., J. Physiol.*, 1922, **56**, xliv.
' Bacterial Products (? Accessory Factors) in Relation to Bacterial Growth.' *Ibid.*, 1922, **56**, xlv.

Studies in Immunity.

At St. Mary's Hospital, London, Sir Almroth Wright, F.R.S., has continued to receive a whole-time grant from the Council. Reference was made in the previous Report to the appearance of the revised edition of his book on ' The Technique of the Teat and Capillary Glass Tube ' for the preparation of which much of Sir Almroth Wright's recent work has been done. He has also been actively continuing his studies of immunization which show that it is possible to obtain an immediate development of protective substances by intravascular inoculation, and that this phenomenon can be reproduced in healthy shed blood *in vitro*.

It is also possible by this ' vaccine response test ' to ascertain by simple means *in vitro* whether a patient is or is not capable of responding to inoculation, and to determine the optimum dose. To take part in the further development of this important investigation, Dr. Leonard Colebrook, a member of the Council's staff, has temporarily left the National Institute for Medical Research to work at St. Mary's Hospital. Work on the physical phenomena of ' intertraction ' observed by Sir Almroth Wright, as mentioned in the previous Report, has been continued in his laboratory by Dr. Schoneboom, and the observation has been shown to apply to every kind of chemical substance.

Dr. E. H. Kettle has continued to receive a part-time grant for work at St. Mary's Hospital, London, in collaboration with Dr. W. E. Gye of the Council's scientific staff at the National Institute. They have followed up their previous discovery that the local virulence of the tubercle bacillus in the tissues is increased in the presence of silica, as already mentioned on p. 21. This experimental work has an important bearing on Miners' Phthisis, as was pointed out in the previous Report. Dr. Kettle has also made observations upon fibrosis of the liver and kidneys in man, for a comparison with those made in experimental work by Dr. Gye and Dr. Purdy at the National Institute.

At the University and Western Infirmary, Glasgow, Dr. James Learmonth is investigating the possibility of the transmission of acquired protective substances in the blood in a rapidly breeding animal, and he is also examining cancerous and precancerous tissues for the iodophil substances described by Mr. C. J. Bond. The Council are making a grant for part-time work and for special expenses.

Carriers of Enteric Disease.

As mentioned in the previous Report, an inquiry into this subject was undertaken at the request of the Scottish Board of Health, who have made cases available for study. The work is under the general direction of Professor R. Muir, F.R.S., and Professor C. H. Browning at the University of Glasgow, and the Council are making a grant to Dr. R. Smith for continuing the investigations begun last year by Dr. H. L. Coulthard. With Dr. W. McKendrick the local reaction to intradermal injections of small doses of typhoid and paratyphoid A and B vaccines have been studied in the carriers and in 14 cases of acute enteric infections. Control tests have been made upon inoculated persons and on 360 individuals suffering from other febrile conditions. The results indicate (1) that in non-enteric conditions positive reactions do not occur, (2) that a positive reaction is so commonly given by known carriers that they have definite value for the discovery of the carrier condition, and (3) that the test enables typhoid and paratyphoid infections to be distinguished.

Curative trials have been made of the methods of altering the intestinal bacteria by the administration of cultures of *B. acidophilus* in milk. It has not been found possible to modify the excretion by carriers of viable typhoid bacilli by this means.

Food Poisoning.

For the assistance of the Ministry of Health and in consultation with Dr. MacFadden of the Food Department of the Ministry the Council have maintained the whole-time grant made to Mr. P. Bruce White for work on this subject in Professor Walker Hall's laboratory in the University of Bristol under a scheme of inquiry arranged by Dr. W. G. Savage, Medical Officer of Health for Somerset. Arrangements have been made by the Ministry of Health and by the Scottish Board of Health under which food materials for special investigation are supplied from outbreaks of bacterial food-poisoning throughout Great Britain. The material recently examined by Mr. White has included that from the cases of poisoning by *B. botulinus* which occurred at Loch Maree during the past summer, and nearly fifty other outbreaks of various kinds have come under observation during the year. As part of these inquiries Mr. White has also bacteriologically examined many rats from slaughter-houses and other places associated with food, and has investigated certain outbreaks of disease among live stock. He is also studying the characters and interrelationship of the organisms of the Salmonella group, which are frequently concerned in cases of food-poisoning.

Infections of the Alimentary Tract.

The grant to Dr. F. H. Teale has been maintained for the expenses of work at University College Hospital, London, upon infections of the alimentary tract and the portals of their entry, and upon the degree of immunity which can be produced by bacteria in the food. The results which he has so far obtained are not in accord with those published by Besredka, whose experiments he has been repeating. With Dr. Dennis Embleton he has also been investigating a filterable virus of common cold.

F. H. Teale—
'Paths of Infection. III. Alimentary Infection.' (In the press.)

Epidemic Infantile Diarrhoea.

Special arrangements were made during the past summer and autumn for a study of this frequently fatal disease, at the suggestion of members of the staff of the Great Ormond Street Hospital for Children, London. The short period of the year during which it occurs typically has always made investigation difficult, and preparations for an inquiry were made in advance. Complete facilities were granted by the authorities of the hospital, who held beds available for cases and allowed the Council to equip

a temporary laboratory. Dr. Donald Paterson, a member of the hospital staff, was in charge on the clinical side, Dr. G. M. Findlay of the University of Edinburgh was responsible for the bacteriological and serological work, and Dr. J. C. Spence of Newcastle-on-Tyne was biochemist; in addition, Dr. M. H. Gordon of St. Bartholomew's Hospital and Dr. D. Nabarro, pathologist at Great Ormond Street, were available for special investigations. It so happened, however, that the disease was happily rare in the past cold and rainy summer, and that only six true cases became available for observation. Valuable work was nevertheless done by Dr. Paterson, Dr. Findlay, and Dr. Spence in the examination of normal infants as controls and in working out lines of investigation for a future epidemic season. They were also able to make a more complete study of 'coeliac disease' in children, of which the results will shortly be published. The Council are greatly indebted to Dr. Nabarro and Dr. Paterson, and to the Secretary and authorities of the hospital for their cordial co-operation in these inquiries.

The 'Bacteriophage' Phenomenon.

At the Brown Institution, University of London, Dr. F. W. Twort has continued his well-known work on this subject on the lines mentioned in previous Reports. He is now returning to the study of vaccinia (small-pox) in relation to the general scheme of work on filterable viruses to which reference has already been made (p. 11). The Council are making a part-time grant and providing special expenses.

F. W. Twort—

'The Bacteriophage: The Breaking Down of Bacteria by Associated Filter-Passing Lysins.' *Brit. M. J.*, 19th August 1922.

'A Theoretical Study of the Nature of Ultramicroscope Viruses.' *The Veterinary Journal*, August and September 1922.

Fatty Degeneration.

The whole-time grant to Dr. T. Rettie for work with Professor J. Lorrain Smith, University of Edinburgh, has been maintained. By means of mordanting with aldehydes they have obtained a staining method which reveals histological differences between fat deposited by normal metabolic processes and fat due to degenerative processes in the body tissues. The following papers have been published:

J. Lorrain Smith and T. Rettie—

'Further Notes on the Staining Reactions of Fat and Lipins in Tissue Sections.' *J. Path. & Bacteriol.*, 1922, **25**, 403.

'Staining Reactions of Fat in Tissue Sections.' *Ibid.*, 1922, **25**, 143.

Intestinal Stasis.

A grant for the special expenses of work on this subject has recently been made to Dr. Louis Gross. The investigation is being

carried out in Sir Arthur Keith's laboratory at the Royal College of Surgeons and in Professor Starling's laboratory at University College, London.

Status Lymphaticus.

The Committee (p. 115) appointed jointly with the Pathological Society of Great Britain and Ireland continue to collect information as cases come to the notice of their members. Professor E. Emrys-Roberts, University College, Cardiff, acts as Secretary, and the clerical and other expenses are defrayed by the Council.

Paget's Disease.

At the London Hospital, Mr. W. S. Perrin has nearly concluded investigations into the pathology of Paget's disease of the breast, based on material from thirty cases, and into the clinical value and scope of the injection method of treating haemorrhoids. The Council are making a grant for part-time work and for expenses.

Studies in Morbid Anatomy.

The Council are making a grant for the expenses of various investigations carried out or directed by Professor H. M. Turnbull at the London Hospital. He has himself investigated the sites of tuberculous infection as already mentioned (p. 77), has made histological examinations of specimens for the Salvarsan Committee (p. 85), and has given invaluable assistance to many other investigations for the Council. The work of Mr. A. C. Palmer (p. 50) and of Mr. W. S. Perrin, just mentioned, is being done under his general direction.

Post-operative Gastro-jejunal Ulceration.

Expenses have been provided for experimental work on this subject by Mr. J. Mill Renton, University of Glasgow. His results show that, among possible mechanical causes of ulceration following the operation of gastro-enterostomy, the use of non-absorbable material for the Lembert or outer suture, as distinct from the customary absorbable inner suture, may be important.

Pedigrees of Anomalies and Diseases of the Eye.

The whole-time grant to Dr. Julia Bell for work on this subject under the direction of Professor Karl Pearson, at the Galton Laboratory, University of London, has been maintained, and the first instalment of the results has appeared in the following volume :

Julia Bell—
The Treasury of Human Inheritance (*II*). *Anomalies and Diseases of the Eye* (*i*). (*Nettleship Memorial Volume.*) Cambridge University Press, 1922.

Spirochaetosis.

Special expenses are being provided for work on spirochaetosis of the stomach by Professor J. S. Edkins of Bedford College, London, and for work on *Spirochaeta morsus muris* by Dr. T. Joekes at St. Bartholomew's Hospital, London.

Trypanosome Infections, &c.

With the concurrence of the Colonial Office, further expenses have been allowed to Dr. H. Lyndhurst Duke, Government Bacteriologist in Uganda.

Blood Protozoa.

Working at the Wellcome Bureau of Scientific Research with a whole-time grant from the Council, Mr. Cecil A. Hoare has obtained interesting results in a study of trypanosomiasis in British sheep, a condition of which the existence in this country had previously been denied. He has found that a trypanosome is commonly present in small numbers in the blood of British sheep, that it is identical with the flagellate *Crithidia melophagia* (now renamed *Trypanosoma melophagium* in accordance with the rules of Zoological nomenclature) with which the sheep-ked (*Melophagus ovinus*) is so frequently infected, and that the infection may be transmitted from sheep to sheep by the ecto-parasitic ked. The full results so far obtained will shortly be published.

Experimental Epidemiology.

In the previous report reference in some detail was made to Dr. W. W. C. Topley's important studies of the periodicity of experimental epidemics among mice. This work, begun early in 1918, has continued to make progress, although temporarily interrupted during the past summer by removal from Charing Cross Hospital, London, to the University of Manchester, on Dr. Topley's appointment there to the Chair of Hygiene. The Council are maintaining their grant for the expenses of the work and are providing the assistance of Miss J. Ayrton, who has taken the place of Dr. G. Selby Wilson on his retirement from the work owing to ill health.

During the past year the course of events during the pre-epidemic phase of the spread of infection has been particularly studied, and experiments have been carried out to test the effect of dispersing a population, which has been exposed to the risk of infection, into several small groups. It has been found that, during the pre-epidemic stage of the spread of bacterial infection among mice, single deaths, or small groups of deaths, due to the specific infection studied, occur at considerable intervals before the rise of the main epidemic wave and afford a warning that

such a wave is at hand. In many cases, also, there has been observed during the same period an increase in the daily mortality from all causes.

The results obtained in the experiments on dispersal indicate that, if a mouse-population which has been exposed to the risk of infection be dispersed into several small groups during the pre-epidemic phase, the total mortality is far less than if the animals be retained as a single large group. It appears that, if the small groups be later combined into a single aggregate, further deaths may occur ; but the total mortality in a group of mice, which has been dispersed and then re-accumulated, is notably less than that in a similar group which has been retained throughout as a single unit of population. It seems already that it might be of value tentatively to apply the principles suggested by these experiments to natural epidemics occurring among live stock, especially such stock as poultry, where there are large ' herds ' of relatively small individuals. In order to limit, for instance, the ravages of a given epidemic, trial might be made of dispersal into small groups at the first sign of an outbreak of disease, followed by re-accumulation into groups of more convenient size after a given interval.

Reports on these experiments will soon be published, and the information already obtained strongly suggests that the whole question of the immunity of a herd, as contrasted with the immunity of the separate individuals of which it is made up, will repay careful and extensive study.

During the present year a series of papers have appeared in the *Journal of Experimental Medicine* which report the interesting results obtained in a parallel investigation in experimental epidemiology which has been conducted, during the past four and a half years, at the Rockefeller Institute in New York. These experiments were begun quite independently of Professor Topley's contemporary work, but they necessarily cover closely similar ground, and it is therefore possible to make an instructive comparison of the results obtained. So far as this can be done the results are in close agreement, and more especially as regards the tendency for long-continued epidemics to occur in a series of waves, and the fate of those mice, which, having passed through one such wave, are exposed to the risk of infection during a later wave.

W. W. C. Topley—
' The Spread of Bacterial Infection. Some Characteristics of the Pre-epidemic Phase.' *J. Hyg.*, 1922, **21**, 10.
' The Spread of Bacterial Infection. The Effect of Dispersal during the Pre-epidemic Stage, and of consequent Re-aggregation.' *Ibid.*, 1922, **21**, 20.
W. W. C. Topley and H. A. Fielden—
' The Succession of Dominant Species in a Mixed Bacterial Culture in a Fluid Medium.' *Lancet*, 2nd December 1922.

Metazoan Parasitology.

Structure and Infections of Lice and Ticks.

At the Molteno Institute of Parasitology, University of Cambridge, Dr. D. Keilin has continued the work for which the Council make a part-time grant by arrangement with the Beit Memorial Trustees. A part-time grant is now also being made to Mr. L. G. Saunders for work in the same laboratory. Both investigations are being carried out under the general direction of Professor G. H. F. Nuttall, and their scope is sufficiently indicated by the titles of the following papers :

D. Keilin—

'On Some Dipterous Larvae infesting the Bronchial Chambers of Landcrabs.' *Annals and Mag. of Natural History*, 1921, Ser. 9, **8**, 501.

'On the Life History of *Dasyhelea obscura* Winn. (Diptera, Nematocera, Ceratopogonidae) with some remarks on the Parasites and Hereditary Bacterian Symbiont of this Midge.' *Ibid.*, 1921, Ser. 9, **8**, 576.

'On the Calcium Carbonate and the Calcospherites in the Malpighian tubes and the Fat Body of the Dipterous Larvae and the Ecdysial Elimination of these Products of Excretion.' *Q. J. of Microscop. Science*, 1921, **65**, 611.

'On a Ciliate : *Lambornella stegomyiae* n.g., n.sp., parasitic in the body cavity of the larvae of *Stegomyia scutellaris* Walker (Diptera, Nematocera, Culicidae).' *Parasitology*, 1921, **13**, 216.

'On a New Type of Fungus : *Coelomomyces stegomyiae* n.g., n.sp., parasitic in the body cavity of the larvae *Stegomyia scutellaris* Walker (Diptera, Nematocera, Culicidae). *Ibid.*, 1921, **13**, 227.

L. G. Saunders—

'The Comparative Morphology of the Larvae and Pupae of Four Terrestrial Ceratopogonid midges.' (In the press.)

Worm Infections.

A grant has again been made for the special expenses of work by Professor R. T. Leiper at the School of Tropical Medicine, London, and the Council are also providing the whole-time assistance of Miss G. Z. L. Le Bas. The problem which Dr. Leiper has now particularly in view is the study of the toxic substances by means of which helminth parasites induce disease in their 'hosts'.

VI. INDUSTRIAL MEDICINE AND INDUSTRIAL FATIGUE.

Miscellaneous Researches into Industrial Diseases.

Dust Inhalation and Pulmonary Disease.

The Council have again provided special expenses for further experimental work on this subject by Dr. J. S. Haldane, F.R.S., at the University of Oxford.

Work on silicosis by Dr. W. E. Gye, Dr. E. H. Kettle, and Dr. W. J. Purdy has already been mentioned under another heading (p. 21).

Miners' Nystagmus.

The Committee (p. 114) appointed to deal with this subject have now issued their first report, and this has been published. The investigations have included the clinical examination by Dr. T. L. Llewellyn, Secretary of the Committee, of two thousand cases from all parts of the kingdom, investigations by Mr. G. H. Pooley, F.R.C.S., of Sheffield, into the relationship of miners' nystagmus to errors of refraction in the eye, studies by Dr. H. W. Eddison, formerly working for the Committee with a grant from the Council, of the psycho-neurotic factors of the disease, observations by Dr. Llewellyn of the underground conditions in mines showing a high incidence of nystagmus, photometric tests made underground, and trials of electric cap lamps in several collieries.

The Committee find that the prime factor in the production of miners' nystagmus is deficient illumination, especially in the case of workers at the coal face, and that this is in turn due to the low illuminating power of the safety lamps in general use and the distance at which these have to be placed from the objects to be lit. These and their other conclusions are given fully in their Report.

' First Report of the Miners' Nystagmus Committee.' *M. R. C. Special Report Series*, No. 65, 1922.

Miners' 'Beat Knee', 'Beat Hand', and 'Beat Elbow'.

Dr. T. L. Llewellyn and Professor E. L. Collis have undertaken a preliminary investigation for the Council into these three conditions, technically known as subcutaneous cellulitis over the patella, subcutaneous cellulitis of the hand, and acute bursitis over the elbow, respectively, with a view to advising what, if any, new research work is practicable and desirable for the assistance of the Mines Department.

Ankylostomiasis in Cornish Miners.

Further results have now been published of the work done last year, and mentioned in the previous Report, by Professor R. T. Leiper (p. 103) and his assistants.

The Incidence of Occupational Diseases.

Work on this subject has now been entrusted to the Committee on Industrial Health Statistics mentioned below.

An investigation into the occupational incidence of cancer has already been mentioned (p. 30).

The Industrial Fatigue Research Board.

The unprecedented trade depression prevailing throughout the past year has greatly affected the work of the Industrial Fatigue Research Board, and has prevented the full development of the schemes foreshadowed in their Second Annual Report. On the other hand, advantage has been taken of this abnormal period to gain knowledge of the effects of short time and of the changes in the usual incentives in industrial work.

A detailed account will be given by the Board in their Annual Report. Brief reference, however, should be made here to the various investigations completed during the year or now in progress.

Committee on Industrial Health Statistics.

The Committee have given much time to the critical examination of numerical data collected in various investigations. Questions of co-operation with certain industries with a view to the keeping of current sickness records upon a system allowing effective statistical treatment are now under consideration.

Miss E. M. Newbold is engaged in a study of the personal factors in accident causation, based upon statistical treatment of existing accident records. In this the full co-operation of many industrial firms has been secured. At a later stage it is proposed that the investigation shall be combined with a psychological inquiry into the qualities that make for susceptibility to accident.

As long ago as 1872, the late T. A. Welton (*Journ. Inst. Act.*, 1872, xvi) called attention to the probable effects of migration in modifying rates of mortality in urban and rural districts. Of recent years some distinguished epidemiologists, notably Dr. W. H. Hamer, have attached great importance to this factor, and have attributed to it a significant share of the rise or decline of phthisis mortality. To obtain exact data bearing upon the question involves a careful local study of the death-rates, at different ages of migrant and non-migrant members of rural families. It appeared to the Council that valuable information of this type might be obtainable through the co-operation of the parochial clergy. Owing to the kindness of the Bishop of Chelmsford, the Council have been fortunate enough to secure the co-operation of the Rev. H. Iselin, Rector of Rawreth, Essex. Mr. Iselin has already collected some interesting particulars about the movement of population from the rural parishes of the diocese, and it is hoped

that the inquiry, which must necessarily be a protracted one, will throw some light upon the differential death-rates of migrant and non-migrant members of rural families.

E. A. Rusher—
'The Statistics of Industrial Morbidity in Great Britain.' *J. Roy. Stat. Soc.*, 1922, **85**, 27.

Committee on Physiology of Muscular Work.

The vacancy on the Committee caused by the death of Professor F. A. Bainbridge, F.R.S., referred to last year, has been filled by the appointment of Professor M. S. Pembrey, F.R.S.

At the University of Manchester, Mr. Hartley Lupton, working under the supervision of Professor A. V. Hill, F.R.S., has gained important new knowledge of the effects of heavy muscular exercise, based on measurement of the rates of oxidative recovery after work. The research is being continued.

Mr. W. Hartree is also continuing his work at the University of Cambridge on the physiology of muscle in collaboration with Professor A. V. Hill, and the papers mentioned below have been published. The Council's part-time grant is being maintained.

At the University of Glasgow, Professor E. P. Cathcart, F.R.S., with the assistance of Miss E. Bedale and Mr. G. McCallum has been studying the efficiencies of different muscles and the 'static component' in muscular work.

At Guy's Hospital, Professor M. S. Pembrey, F.R.S., Dr. G. H. Hunt, Mr. W. D. Hambly, and Mr. E. C. Warner have been engaged in the study of different tests for physical fitness with a view to their practical application (p. 48).

At Oxford, Dr. H. M. Vernon has completed an investigation of the influence of rest pauses and changes of posture upon the onset and degree of fatigue in muscular work involving maximal effort.

Hartley Lupton—
'The Relation between the External Work Produced and the Time Occupied in a Single Muscular Contraction in Man.' *J. Physiol.*, 1922, **57**, 68.
'The Recovery Oxygen-usage after Exercise in Man.' *Proc. Physiol. Soc., J. Physiol.*, 1922, **56**, xvii.
A. V. Hill and H. Lupton—
'The Oxygen Consumption during Running.' *Ibid.*, 1922, **56**, xxxii.
M. S. Pembrey and Others—
'Tests for Physical Efficiency, Part I.' *Guy's Hospital Report.*
'Tests for Physical Efficiency, Part II.' *Ibid.*
W. D. Hambly and B. A. McSwiney—
'The U-tube Manometer with Relation to Muscular Exercise.' *Proc. Physiol. Soc., J. Physiol.*, 1922, **57**, i.
W. Hartree and A. V. Hill—
'The Nature of the Isometric Twitch.' *J. Physiol.*, 1921, **55**, 389.
'The Heat-production and the Mechanism of the Veratrine Contraction.' *Ibid.*, 1922, **56**, 294.
'The Recovery Heat-production in Isolated Muscles.' *Proc. Physiol. Soc., J. Physiol.*, 1922, **56**, xxiii.
'The Recovery Heat-production in Muscle.' *J. Physiol.*, 1922, **56**, 367.
H. M. Vernon—
'The Influence of Rest Pauses and Changes of Posture on the Capacity for Muscular Work.' *Ibid.*, 1922, **56**, xlvii.

Committee on the Industrial Physiology of the Respiratory and Cardio-Vascular Systems.

The Committee have had before them various Reports from the Board dealing with the effects of atmospheric conditions upon industrial work.

Work at the National Institute for Medical Research on the relation of atmospheric conditions, particularly of cooling power, to physical efficiency has already been mentioned (p. 25).

L. Hill, H. M. Vernon, and D. Hargood-Ash—
'The Kata-thermometer as a Measure of Ventilation.' *Proc. Roy. Soc.*, 1922, B. 93, 198.

Committee on Industrial Psychology.

The Committee have given consideration to the data which have been collected by psychological methods in the silk and laundry trades, and they have generally supervised the following researches.

At the University of Cambridge, Miss M. Vernon, working under Mr. F. C. Bartlett, is exploring by laboratory methods the personal factors in accident causation, on lines in general similar to those formerly adopted by Mr. B. Muscio. Mr. Bartlett has made arrangements to investigate a problem referred to the Board by the Post Office and H.M. Stationery Office, namely, that of finding the optimum contrasts between coloured inks and various papers, of kinds suitable for official forms of return. In the same laboratory, Miss S. M. Sowton, under the direction of Dr. C. S. Myers, F.R.S., is engaged in researches upon the psychological effects of the menstrual period.

At Manchester University, under the supervision of Professor T. H. Pear, Miss I. Burnett is studying the optimum spell for monotonous work, and work involving mental rather than muscular effort. Mr. James A. Fraser is engaged, also under Professor Pear, in studies of the intelligence and special aptitudes required in the occupation of weaving.

An important inquiry into modes of vocational guidance has recently been undertaken by Mr. Cyril Burt in co-operation with Miss May Smith and Miss Frances Gaw. The work is being done with the active co-operation of the National Institute of Industrial Psychology and with assistance from the Ministry of Labour and the London County Council Education Authority.

B. Muscio—
'Motor Capacity with Special Reference to Vocational Guidance.' *Brit. J. Psych.*, 1922, **13**, 157.

Industrial Investigations.

In the textile industries several important investigations have been completed. Mr. S. Wyatt, assisted by Mr. A. D. Ogden, has dealt with variations in efficiency in weaving and their relation to environmental and other factors. He has also explored the atmospheric conditions in weaving sheds in summer and winter

by means of the kata-thermometer and in this way has made a substantial contribution to the knowledge of physiological effects of artificial humidification, a subject which has been before the trade for many years. With a similar object Mr. H. C. Weston has investigated the more extreme conditions prevailing in the fine linen weaving industry. A report by Mr. P. M. Elton, upon the extent and causes of individual differences in weaving efficiency in the silk industry has been generously placed at the disposal of the Board by Messrs. Grout & Co., Ltd., Great Yarmouth, who defrayed its cost.

In the pottery industry, Dr. H. M. Vernon, assisted by Mr. T. Bedford, has investigated the prevalence of high temperatures in various departments of work and has made suggestions for improving the conditions.

In the laundry trade, Miss M. Smith, assisted by Miss Baker, has studied the variations in working capacity associated with different conditions of working hours and environment.

In the glass trade, an investigation is being conducted by Mr. E. Farmer (assisted by Mr. E. G. Chambers) into the relation of hours of work to efficiency and allied questions.

Finally, a series of questions relating to Post Office work has been referred to the Board by H.M. Postmaster-General. In the first instance, an investigation is being conducted by Mr. E. Farmer and Miss May Smith, under the direction of a special committee, into the nature and causes of telegraphists' cramp.

In addition to these special studies, others dealing with subjects of a general nature and covering a wider field are now beginning. The optimum lengths of spell and the most suitable arrangement of rest-pauses for industrial work of different types are being specially investigated by Dr. H. M. Vernon, assisted by Mr. T. Bedford, and information in these directions is being gained by the other investigators in the course of their special work. A preliminary inquiry into the relation of machine design to the fatigue and discomfort of the worker is being conducted by Mr. H. C. Weston.

Third Annual Report of the Industrial Fatigue Research Board. (In the press.)

P. M. Elton—
'An Analysis of the Individual Differences in the Output of Silk-Weavers.' *Reports of the Ind. Fat. Res. Board*, No. 17, 1922.

H. M. Vernon and T. Bedford—
'Two Investigations in Potters' Shops. *Ibid.*, No. 18, 1922.

H. M. Vernon and B. Muscio—
'Two Contributions to the Study of Accident Causation.' *Ibid.*, No. 19, 1922.

H. C. Weston—
'A Study of Efficiency in Fine Linen Weaving.' *Ibid.*, No. 20, 1922.

May Smith—
'Some Studies in the Laundry Industry.' *Ibid.*, No. 22, 1922.

S. Wyatt—
'Atmospheric Conditions in Cotton Weaving.' *Ibid.*, No. 21, 1922.
'Variations in Efficiency in Cotton Weaving.' *Ibid.*, No. 23, 1922.

T. Bedford—
'The Ideal Work Curve.' *J. Ind. Hyg.*, 1922, **4**, 235.

VII. CONCLUSION.

In a previous Annual Report the Council made reference to the munificent endowment of nearly one and a quarter million pounds given early in 1920 to the University College and Hospital in the University of London, by the Board of the Rockefeller Foundation of New York, and they pointed then to the special value and significance of this gift. During the past year the Foundation have made further proposals of the most important and generous kind, likely to have as notable an influence in another direction upon the progress of the medical sciences in this country. They have offered two million dollars to the Government for the purchase of a site and the erection of a building for a great School of Hygiene in association with the University of London. The Government have accepted this offer and have undertaken to provide for the sufficient maintenance of the building and the School. It is intended that this should be a centre for post-graduate instruction in hygiene and the practice of preventive medicine, and no less for research work in the connected branches of science. It is intended, too, that it should promote both by education and research the best interests of the preventive services of medicine not only in this country but in the various parts of the Empire as a whole.

The special circumstances in which these gifts from the United States have been made and the spirit of international goodwill and co-operation to which they testify, make it all the more gratifying that important endowments should have come recently from within our own country to the sciences of medicine, and to some of these the Council cannot refrain from alluding briefly here.

The trustees of Sir William Dunn's residuary estate have made a remarkable series of benefactions to medicine. Shortly before the war they had included among their grants the sum of £23,000 for the permanent endowment of a Chair of Pathology at Guy's Hospital, London. Two years ago, in recognition of the fundamental position of biochemistry among the sciences serving medical progress, and of the urgent need for the training of more biochemists, they gave a sum exceeding £200,000 to the University of Cambridge for the endowment there of a Chair of Biochemistry and the erection of a School of Biochemistry, with permanent provision for the maintenance of the building and for an important part of the necessary expenditure upon research work. In the present year the Dunn Trustees have brought further aid to the position and prospects of pathological science in our country by giving £100,000 to the University of Oxford for the building and maintenance of a new School of Pathology, and they have contributed in addition the estimated cost of converting the present pathological building into a com-

pletely adequate School of Pharmacology. The Trustees, finally, have given in recent months the first important financial help which has come from any private British source to the new units of medicine and surgery which are destined to play so indispensable a part at the chief London Hospitals in the advancement of clinical medicine by research. They have provided for the construction and equipment of either new or improved laboratories for the special service of the Clinical Units in St. Bartholomew's Hospital, St. Thomas's Hospital, and the London Hospital.

The Council would venture to pay here the most cordial recognition to this remarkable series of timely and correlated benefactions, not only from a sense of their intrinsic and permanent value but from the knowledge that they will bring the most direct and early assistance in many of its chief parts to the work which the Council are charged to promote. They recognize, too, that these gifts mark a growing recognition by men prominent in practical affairs that aid given to the primary sciences from which all future progress in medicine must spring, is truly charitable aid, and that there is no other way of contributing securely to those permanent diminutions of human suffering that only new knowledge and power, gained by research, can bring. A new piece of knowledge in the light of which any diminution of pain or loss can be made possible in permanence for all men at all times must have a value which in the literal sense of the word is infinite ; the necessary search for it must have a claim upon enlightened charity at least as great as any present individual needs for palliative relief.

Other important benefactions to medical science have been made in the past year. Under the will of the late Miss Foulerton a sum of over £80,000, including a former gift, has come to the Royal Society for the endowment, at the discretion of the Society, of research work for the improvement of medicine. For researches into cancer Lord Atholstan has recently given £20,000 to the Imperial Cancer Research Fund, and Sir William Veno £10,000 to the Cancer Research Department of the Middlesex Hospital.

The Council would refer lastly to a gift to scientific work in which they find special significance. The Panel Committee of Sheffield have contributed £1,000 to the University of Sheffield towards the provision and equipment of the Field Laboratories which have been erected by the University close to the city. In these is being done the experimental work upon various dietetic problems in relation to growth and disease, and more particularly to rickets and to Graves's disease (exophthalmic goitre), which has been mentioned already on pp. 56, 68. The Council have supported this work from its beginning, and it is specially gratifying to find that men engaged in medical practice, who can see it and its results at close quarters, have been willing

to give testimony to its practical value like that shown in this purely voluntary and spontaneous financial aid.

The Council are unwilling to close this account without reference to the great loss their work has suffered during the year by the sudden and untimely death of Dr. W. H. R. Rivers, F.R.S. His well-known earlier work in the fields of neurology and experimental psychology had allowed him to make almost unique contributions to the study of anthropology, and to this he had brought new strength from the methods and results of those other sciences. During the war he gave inestimable service when he turned his attention to the numerous psychological problems made prominent in warfare and to the study of the neuroses associated with fighting and strain. The opportunities that then fell to him brought into full use his stores of knowledge, while his powers and confidence seemed to come to a new maturity. Great as his actual achievements had been, even higher expectations had been formed for his future work. The Council have peculiar reason for deploring the withdrawal of his help and for treasuring his memory. His military service in the war was given in association with them; both then and later he had been assisting in almost every week some part of the work of the Council, either in the study of mental disorders or in the physiology of the sense organs, and upon occasion in secondary problems like those, for instance, of miners' nystagmus. Upon the side of psychology he greatly aided the schemes of the Industrial Fatigue Research Board, and at the moment of his death he was engaged in a piece of work for their Committee upon Industrial Psychology. His very rare qualities of mind and judgement make it impossible to hope that his place can be filled.

GOSCHEN,
Chairman of the Council.

WALTER M. FLETCHER,
Secretary of the Council,

15, York Buildings,
Adelphi,
London, W.C. 2. *30th November*, 1922.

APPENDIX.

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(*Sub-Committees at present organized under a Committee of the Council, of which* Dr. A. S. MacNalty *is the Secretary.*)

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J. Macintosh.
H. H. Thomson, M.D.
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G. T. Western, M.D.
Professor T. B. Wood, C.B.E., F.R.S.

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Professor S. L. Cummins, C.B., C.M.G., late A.M.S.
A. Stanley Griffith, M.D.
A. C. Inman, M.B.
A. S. MacNalty, M.D.

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Scottish Committee.

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T. Y. Finlay, M.D.
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The Intestinal Protozoa of Man. By Clifford Dobell, and F. W. O'Connor. Price 15*s.* net. [Bale, Sons & Danielsson, Ltd.]

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